ANNALS OF SURGERY

VOL. 106 JULY, 1937 No. 1

INFECTIONS OF THE DANGEROUS AREAS OF THE FACE

THEIR PATHOLOGY AND TREATMENT

URBAN MAES, M.D.

NEW ORLEANS, LA.

FROM THE DEPARTMENT OF SURGERY OF THE SCHOOL OF MEDICINE OF LOUISIANA STATE UNIVERSITY, AND THE SURGICAL SERVICES OF CHARITY HOSPITAL AND TOURO INFIRMARY, NEW ORLEANS, LA.

INFECTIONS of the "dangerous area" of the face were first mentioned in the literature in 1852, when Ludlow[8] described six cases, three of them fatal. The first patient, a moderately stout man of 20, scratched the head off a pimple on his lip six days before admission to the hospital and died 36 hours after admission, in spite of the use of compresses, sedatives and leeches. The second patient, another moderately stout man of 36, cut a pimple on his lip while shaving seven days before admission to the hospital; he died four days after admission, in spite of treatment by multiple incisions, compresses, sedatives and leeches. The third patient, a man of 19, developed a small boil on the upper lip five days before he entered the hospital; he was treated by multiple incisions, from which practically no pus was obtained; he died on the fifth day. In the first case autopsy revealed a purulent exudate in the lungs and kidneys; in the last it revealed multiple lung abscesses and mediastinitis. In neither case was the head examined.

While Ludlow's theory of the epidemic character of carbuncular inflammation is, of course, entirely outmoded and discarded today, a good deal else that he says is worthy of respectful attention. After describing the condition as "a local mischief upon which constitutional disturbances supervene," he notes that in all the fatal cases there was first a period of inflammation with great pain, followed by a period of mortification with diminution and partial cessation of pain, the inflammation spreading widely but "receding from parts whose vitality had suffered and from tissues struck with death." He realizes that it is the circulation of morbid matter and not the mere inflammation in the external parts which is responsible for the fatality. He doubts whether, if one incision is unavailing, it is judicious to practice others, since local measures "demolish the feeble bulwarks which oppose the spread of the disease."

The aim of the physician should be not directly to cure the disease but rather to support the patient during its continuance, "to animate nature in

Submitted for publication, October 21, 1936.

the struggle and to enable her to throw off her antagonist." Those are sound observations, we repeat, and many of them might still be taken to heart, even though the fundamental explanation of the disease is incorrect. It could scarcely have been correct. For one thing, the head, in which lay the key to the mystery, was not examined in either case in which autopsy was permitted, and even if it had been, this was before the days of applied bacteriology and the thrombophlebitis and thrombosis which would undoubtedly have been found but which could not possibly have been interpreted correctly.

Thirty-one years later, in 1883, Sir Frederick Treves[15] offered the first explanation of why infections in certain areas of the face are so dangerous. After describing the anatomy of the facial vein and its communications, he writes: "These dispositions of the facial vein may serve to explain the mortality of some inflammatory infections of the part. Thus, carbuncle of the face or other diffuse and deep-seated inflammatory conditions, especially of the upper lip and in the neighborhood of the alae nasi, may induce fatal thrombosis of the cerebral sinuses." In another connection he calls attention to the danger of incisions of such inflammations, a warning that has been very generally overlooked.

Almost 30 years more were to pass, however, before this subject began to receive the attention it really deserved. It was in 1922 that Walton Martin[9] wrote what has become the classical paper on this subject. His fear of the facial vein was aroused when he was still a medical student by Treves' warning which we have just quoted, and his interest in the subject was intensified by his own tragic observation of the disease, seven deaths in ten cases. To the explanation Martin advanced practically nothing has since been added. No writer on the subject has been able to do more than to present, in the light of his own experience, what Martin said in 1922.

The "dangerous area" of the face is the triangle which extends roughly from the angles of the mouth to the bridge of the nose, and it is dangerous for purely anatomic and physiologic reasons. The skin of the face is unusually thin for the protective covering of so important an area and is unusually exposed to trauma, particularly in men, who must shave daily. Especially about the mouth and lip it is thickly interwoven with the underlaying muscle fibers, blood vessels and lymphatics, which are here embedded in an unusually small amount of cellular tissue and an unusually large amount of connective tissue. Connective tissue is seldom highly vascularized, but there is a peculiarly rich vascular supply in this area, and the veins are more superficial than they are anywhere else in the body.

The distribution of the venous supply is exceedingly important. The collecting venous trunk for the upper lip ascends along the nasolabial groove to empty into the facial vein at a point at the level of the nostril or the lower border of the orbit. The lower lip is supplied by two rather slender collecting branches which ascend obliquely and the lower of which empties into the facial vein low down in the submaxillary portion. In other words, there is a direct connection between the veins of the lip and the facial vein, which empties into the ophthalmic vein, which communicates, in turn, with the cavern-

ous sinus. The angular vein thus serves to connect the superficial venous system with the deeper intracranial venous channels, furnishing a short and direct pathway from the surface to the interior of the cranium. Access is simplified, furthermore, by the fact that the facial vein has no valves. It should be added, though this pathway is less important, that the anterior facial vein also communicates with the cavernous sinus through the deep facial vein by way of the pterygoid plexus and several emissary veins.

The anatomy and physiology of this region make it abundantly clear why infection in it is so very dangerous. A lesion that would be innocuous elsewhere in the body has the gravest possibilities for ill here. In the first place, all the circumstances militate against localization, the sheet anchor of safety elsewhere in the body. Limitation of motion, which is the first principle of the limitation of the spread of infection, is almost impossible in this region. The taking of every morsel of food, of every drop of liquid, involves motion of the affected area, as do talking, smiling, laughing and crying. It is the most difficult thing in the world, even when speaking has been expressly prohibited, to keep an individual from expressing, almost automatically, his thoughts and needs and desires by words. A conscious endeavor may be made to obey the prohibition, but the facial expression unconsciously changes with one's mental processes, while in delirious and comatose states, which ensue very early in this disease, the patient does not comprehend and cannot heed the warning.

To this important physiologic factor is added an external factor, trauma, which is present in at least 90 per cent of all such cases. It is sometimes absent, but I add myself to the number of those who have never seen a fatal case in which it was not present. The average lay person finds it difficult to refrain from meddling with facial blemishes, and the average doctor seems to find it impossible, whether they are on himself or his patients. It seems something more than a coincidence that this condition should be unusually frequent among medical students and physicians. The lay individual, Martin points out, tampers with his lesion to the accompaniment of grimaces which add to the insult, while physicians use knives, probes or blunt instruments. Whatever the method, the result is the same.

When the factor of trauma is introduced, one of the smaller veins about the lip is almost certain to be injured. Rarely does a great amount of pus escape, and frequently there is none at all. But bleeding does occur, usually into the subcutaneous tissues, where the blood stagnates and makes an excellent culture medium for the bacteria already present, increasing their potency, as Dorst (quoted by Martin) has demonstrated, some 40 times. The wall of leukocytes, upon the integrity of which the limitation of the infection depends, is broken down. Cellular tissue, which accommodates itself well to infection, is practically absent about the lips, as we have pointed out, and connective tissue, which is chiefly present, accommodates itself very badly. The rich venous supply picks up the infection and speedily carries it onward, the speed of the process being accelerated both by motions of the lips and by the absence of valves in the facial vein. A thrombophlebitis is thus readily established

and it is only a short time until there occurs a thrombosis in the vital centers and until there is a massive blood stream infection with the formation of metastatic foci elsewhere if the patient lives long enough. The intracranial thrombosis tends to become bilateral early in the disease because of the close communication between the cavernous sinuses by interlocking venous channels.

The causative agent is practically always the Staphylococcus aureus which finds its natural home in the follicles of the skin and against which even a socially clean face offers no protection. The organisms multiply rapidly and spread widely in the fertile soil in which they find themselves. Lowered resistance on the part of the host of course exerts its usual effect, but there is no need, as was once supposed, to invoke the explanation of the presence of particularly virulent strains of bacteria.

The exact spread of infection in this disease was carefully demonstrated by Logan Turner in 1926. By a series of sections through the nose, the orbit and the base of the skull, he was able to show that the spread to the cavernous sinus was by way of the subcutaneous plexus and the angular and ophthalmic veins. Spread by way of the ptergyoid plexus, as we have pointed out, is anatomically possible but is not usual.

In the first stage of the infection the local lesion resembles the usual carbuncle, furuncle or boil, and the patient has no symptoms at all or merely a slight local discomfort. In the second stage, particularly when unwise manipulations have been undertaken, there is a rapid extension of the process. A wide area of the adjacent tissue is swollen, edematous and indurated. The lip is two or three times normal size and the mouth is opened with difficulty. The skin is reddened, or, if venous stagnation has already occurred, is purplish. The pain is very severe, as the result of tension, and there are chilly sensations, or definite chills, with a mounting fever. In the third stage the swelling is still more extensive. It tends to involve the eyelids, the eye may be completely closed, and exophthalmos may be present. There is a butterfly discoloration of the tissues of the forehead, and the thrombosed veins can be felt beneath the skin as tender, thickened cords. The fever is high, from 105° to 107° F. or even higher, and the pulse is correspondingly elevated, and, to quote Ludlow's original description, "is sharp and powerless." There may be either violent delirium or coma. When the stage of cavernous sinus thrombosis and massive septicemia is reached, the end usually comes promptly. Occasionally the patient dies from pneumonia or from some constitutional state before the characteristic manifestations of the disease have occurred, but this is distinctly unusual. The brief course of the disease, which was noted in Ludlow's first observations, has been corroborated by all subsequent observers.

The matter of diagnosis need not detain us. No physician who has ever seen one of these patients will have the smallest doubt of what is before him. Laboratory studies are usually of only academic interest. A negative blood culture is rarely returned from the laboratory. The uranalysis and blood chemistry are what one would expect in the presence of such an overwhelming infection, as is the blood count. A low leukocytic count means, as always,

a complete lack of resistance on the patient's part, but a high count furnishes nothing in the way of encouragement. Postmortem findings are almost invariably the same, cavernous sinus thrombosis, with or without pyemic manifestations throughout the body.

An outstanding fact about infections of the "dangerous area" of the face is that they occur chiefly in young and vigorous persons. Koslin[7] believes their incidence in persons of this sort is one explanation of their fatal character: such individuals, he says, are scornful of the advice that such apparently minor infections should be cared for in bed or in the hospital.

There is almost no condition in surgery which is so universally mistreated. All methods of treatment are unsatisfactory, but some are far more unsatisfactory than others. The chief trouble, as Martin points out, is that few surgeons see enough cases to arrive at any conclusions on the basis of their own experience. They save or lose one case by some method of treatment and they endeavor to formulate rules on the basis of that case only. Lanz, for instance, saw one of his associates in Kocher's clinic in Berne die from pyemia four days after the incision of a furuncle on his upper lip. It was done in the absence of the great Kocher, it is true, but it was done by an expert. Thenceforth he no longer believed in the surgical treatment of furuncles of the upper lip. Powers saw a young physician in the Chambers Street Hospital die in two days from a boil on the upper lip for which incision was not done. Thenceforth he believed in the early and wide excision of all such lesions. The literature adds to the confusion, partly for the reason we have just noted, partly because authors who report relatively large series of cases fail to make the distinction between mild and severe conditions and also include lesions on all parts of the face and even the neck. The evaluation of any single method of treatment is therefore almost impossible.

Every possible form of therapy has been suggested. Local measures include applications of iodine, mercurochrome, alcohol and similar agents; hot and cold poultices and compresses of various sorts; the injection of carbolic acid; cauterization of the lesion by phenol or the electric cautery; circuminjection of the patient's own blood; Bier's suction; and so on indefinitely. Berndt[2] reports four cases treated by roentgen therapy and Coller[5] believes the method worthy of trial. Hofmann[6] recommends Bier's constricting band around the neck. Brown[3] suggests that all small pimples be covered with adhesive tape to splint them. Suggestions for intravenous therapy include mercurochrome, gentian violet, citric acid and bacteriophage, and specific therapy includes the use of antistreptococcic serum, which seems a singularly illogical method of treatment for a condition primarily staphylococcal in origin.

The chief point of debate is whether or not the lesion should be incised, and I think I may fairly say that the general opinion today is that the less done, the better. Prophylactic measures are naturally best of all. Lay persons must learn to keep their hands off their faces, and physicians must learn to keep their hands off their patients' faces. There can be no objection, of course, to the repeated application of alcohol or some similar drying agent, but manipulations of any sort are strictly contraindicated. If the lesion is

of any but the simplest character bed rest is advised, preferably in the hospital, with nursing care that includes the strict prohibition of speech and laughter. Nourishment is administered with a minimum of disturbance of the parts, and nasal feeding is promptly resorted to if it seems indicated. Opiates and sedatives are prescribed if rest and quiet cannot be secured without them.

Local treatment is limited to the use of compresses. The exact agent used makes little difference, but the method of application is important. Compresses should be small, soft and light, for even in so minor a matter as this the factor of trauma is present. They should be kept constantly warm and moist; Price[11] suggests that fresh solution be added at intervals of 15 minutes with a medicine dropper, a method which involves less disturbance of the parts than the changing of compresses. Care should be taken that the solution is not too hot. I utter this warning advisedly for the pain is frequently so intense that, as I have more than once seen, the patient will burn his fingers as well as his face by his endeavor to relieve it.

All these precautions for so small a lesion may seem to the patient—and to many physicians, I fear—much ado about nothing. They are probably unnecessary in most cases, but their routine use would, I believe, materially reduce the mortality in this highly fatal disease. If the lesion has not been tampered with it is rare indeed that the condition does not clear up without further treatment, or, if necessary, incision can be done later, when localization has definitely occurred.

When thrombophlebitis has once set in, the situation is very different, though I personally believe conservative measures are still best. Ligation of the angular vein was first suggested by Sehileau in 1910 and by Bullock in 1912, and was revived independently by Bailey[1] and by Roeder[12] in 1928. I grant the theoretic correctness of the procedure but I am rather doubtful of its real value, in spite of the successful cases on record. If it is done early, the only time at which its effectiveness is unquestioned, it will be done unnecessarily in most cases. If it is done late, the infection is very likely to have extended beyond the point at which the ligature is applied. Furthermore, as Martin points out, technical difficulties stand in the way of performing the ligation at an appreciable distance from the infected thrombus, and there is real danger, too, of disturbing and loosening the clot by the necessary manipulations. I myself have never seen any early case in which I thought the procedure indicated or a late case in which I thought it would do any good.

When the infection has reached the cavernous sinus I agree with Powell[10] that the physician's chief duty is to permit the patient to settle his worldly affairs before the onset of coma. A few successful cases have been recorded since Dwight suggested surgical invasion of the cavernous sinus in 1900, but they are few indeed; as Chisholm and Watkins[4] observe, only 7 per cent of such patients recover without surgery, but less than 7 per cent recover with it. The same authors add that if the spinal fluid is clear, the patient has a chance for recovery without operation, while if it is cloudy, operation is

frankly hopeless. Martin says that the idea that thrusting a knife into the cavernous sinus might favorably influence the spread of such an infection seems to him to show a singular ignorance of morbid anatomy. Even if the structure were easy of access, meningitis usually follows so closely that cavernous sinus thrombosis can scarcely be considered a surgical condition.

The management of the septicemia and of the meningitis associated with the condition offers few problems which they do not present elsewhere. The chief reliance must be on supportive measures. Various forms of intravenous therapy have been employed, usually without result. Stout,[13] however, reports a personal case in which there were present not only cavernous sinus thrombosis but also staphylococcal septicemia and meningitis, both proved by culture. Staphylolysate was used locally, intravenously and intraspinally, and later, when the patient developed a staphylococcal pyelitis, was injected into the pelvis of the kidney. Complete recovery followed. Staphylolysate was used in one case on my own service a year or two ago; the patient showed considerable temporary improvement, and perhaps if we had used the treatment more courageously, as Stout did, we too might have had a favorable outcome. Since the method is apparently without ill effects, it seems worthy of a trial.

Quite obviously infections of the "dangerous area" of the face, while infrequent, are highly dangerous conditions which should be treated with the greatest fear and respect, no matter how early they are seen and no matter how trifling they may seem. With the proper prophylaxis, and more particularly with the elimination of any sort of trauma, the majority of them will remain innocuous. If the patient does not meddle, if the physician stays his hand, most of them will take care of themselves. This is a condition in which procrastination reaps shining rewards, in which zeal and promptness are attended by fearful consequences. The physician who treats such cases will lose fewer of them if he takes his stand on the firm rock of surgical nihilism. The application of any other method will, as Martin says, "during a long lifetime lead to an astonishing mortality."

SUMMARY OF CASES

During the last nine years at Charity Hospital and during the last six years at Touro Infirmary, there have occurred 20 fatal cases of infections of the "dangerous area" of the face. One patient (at Charity Hospital) was a Negro, this being the only instance of the disease I have ever seen in that race, though why this should be I cannot say. The age range was from seven to 64 years. Fifteen of the patients were between 15 and 28, but one was seven and two were eight years of age, these cases being unusual: the condition does not generally occur before puberty, when the hair follicles and sweat glands reach their full stage of development. Five patients were so seriously ill on admission that no history of any sort could be obtained. Three patients specifically denied trauma; the other 12 patients all gave a history of some sort of manipulation of the lesion, either by their physicians

or by themselves, or by both. All were hopelessly ill, and no method of local or general treatment yielded any but the most transient improvement. Incision and drainage were performed in five cases. In one case, the angular vein on the affected side was tied, in another, bilateral ligation was effected, and in a third, drainage of the cavernous sinus was performed. Death occurred in five hours in one case and in 11 hours in another, and only four patients lived longer than five days. All but one of the blood cultures were positive, and death in all cases was due to cavernous sinus thrombosis with or without septicemia and meningitis.

During this same period four such patients were treated surgically at Charity Hospital with recovery. Two were not very ill, and after the use of conservative measures such as we have outlined, incision and drainage was accomplished without difficulty. Trauma was a factor in both cases. The third patient had a furuncle of the lip which was incised both before and after admission, and her recovery I am inclined to put down as a lucky escape. The fourth patient was admitted in coma with the typical picture of cavernous sinus thrombosis. The sinus was drained immediately by the late Dr. Homer Dupuy, who also tied the left internal carotid artery and removed the left eye. His recovery was stormy but complete, and he presents one of the few instances in which this usually hopeless type of surgery has been successful.

Not strictly pertinent to this subject are certain infections of other areas of the face, the entire extent of which, according to some authorities, should be included in the "dangerous area." We were able to collect a number of such cases while we were searching for the specific fatal cases we have just described, and we include them here because of their related interest. Three are from the records of Touro Infirmary and the remainder from the records of Charity Hospital.

There were two fatal cases of carbuncles of the chin, one in a Negro, both of which had been traumatized. One patient died of septicemia and the other of lateral sinus thrombosis.

There were seven fatal infections of the lower lip, in six of which there was a history of trauma. The other patient was too ill to supply a history. All were desperately ill on admission and died in from three to six days from septicemia, in one case associated with mediastinitis. Incision and drainage was performed in two cases. Infections of the lower lip are generally supposed to be less severe than those of the upper lip because the structures are less mobile, the lip is more efficiently splinted by bone and muscle, and the veins are at a deeper level. That they are very serious, however, these seven cases prove.

There were four fatal cases of cellulitis of the face. One followed a septic sore throat, another followed herpes of both lips, and the origin of the third, in a Negro patient with syphilis and pernicious anemia, is not clear. The fourth patient was too ill to give any history. Incision and drainage was performed in one case. Death was due to septicemia in three cases and to cavernous sinus thrombosis in the fourth.

In three fatal cases the lesion began on the forehead. One patient, 80 years of age, whose furuncle was incised in the accident room on admission, died of arteriosclerotic heart disease, the local lesion probably having nothing to do with the fatal outcome. One of the other patients refused operation; the third died five days after the cavernous sinus had been drained. The cause of death in both cases was septicemia and cavernous sinus thrombosis.

Such infections following extraction of the teeth are supposed to be very unusual but we discovered eight such instances, one of them from Touro Infirmary and the other seven from Charity Hospital. Three were in Negroes, in whom oral hygiene is notoriously poor. One patient died while ligation of the jugular vein was being attempted under ethylene anesthesia, in one case the infected area was incised, though no pus was obtained, and symptomatic measures were used in the other cases. The causes of death included acute mediastinitis, pneumonia, pulmonary edema, septicemia and cavernous sinus thrombosis, the latter complication being responsible for four deaths.

SUMMARY.—(1) The classical paper on infections of the dangerous area of the face was written by Walton Martin in 1922, although our knowledge of the condition dates from Ludlow's description of it in 1852.

(2) The "dangerous area" of the face is the triangle which extends roughly from the angles of the mouth to the bridge of the nose, and it is dangerous for anatomic and physiologic reasons.

(3) These reasons include the thinness of the skin; its constant exposure to trauma; its rich vascular supply, which provides a direct pathway from the surface to the interior of the cranium; the predominance in this area of connective tissue, which adapts itself poorly to infection; and the constant motion of the lips, which militates against any localization of infection.

(4) More important than any of these anatomic and physiologic reasons is the factor of trauma, which is present in 90 per cent of all cases and is introduced by the patient or his physician or both.

(5) The infecting agent is usually the Staphylococcus and the spread is by way of the subcutaneous plexus and the angular and ophthalmic veins. The condition begins as a carbuncle or simple boil. When the factor of trauma is introduced, stagnant blood is provided as a rich culture medium for bacteria, the integrity of the protective leukocytic wall is destroyed, the infection spreads rapidly by way of the rich vascular supply, and the steps of the pathologic process include thrombophlebitis, thrombosis of the cavernous sinus, massive blood stream infection, meningitis, and metastatic abscesses.

(6) The brief course of the disease is characteristic. It begins with a mild local discomfort, followed shortly by extensive swelling, edema and induration of the adjacent tissues. The symptoms and signs after this stage include severe pain, chills, hyperpyrexia, delirium or coma, and prompt death.

(7) The diagnosis is obvious from the history and physical examination.

(8) The condition is universally mistreated. All types of local and intravenous therapy have been advised, but the general opinion now is that con-

servative measures, chiefly absolute rest of the parts, warm compresses, and supportive measures, give the best results, while surgical incision gives the worst. Ligation of the angular vein is theoretically correct but of little practical value, and a few successful operations have been reported for drainage of the affected cavernous sinuses.

(9) Twenty fatal cases of infections of the "dangerous area" of the face are reported, to which are added 24 fatal cases of infection of other areas of the face not usually included in the "dangerous area."

My thanks are due to Dr. M. W. Kaplan, who collected and abstracted the cases from Touro Infirmary.

REFERENCES

[1] Bailey, H.: Ligature of Angular Vein as Preventive Measure in Facial Carbuncles. Surg., Gynec. and Obstet., **46**, 565–567, April, 1928.

[2] Berndt, F.: Treatment of Furuncles and Carbuncles. Zentralbl. f. Chir., **51**, 2686, December 6, 1924. Abstr. J.A.M.A., **84**, 240, January 17, 1925.

[3] Brown, W. G. S.: Cavernous Sinus Thrombosis. Fatal Complication of Minor Facial Sepsis. Lancet, **1**, 960–965, May 2, 1931.

[4] Chisholm, J. J., and Watkins, S. S.: Twelve Cases of Thrombosis of Cavernous Sinus. Arch. Surg., **1**, 483–514, November, 1920.

[5] Coller, F. A., and Yglesias, L.: Infections of Lip and Face. Surg., Gynec. and Obstet., **60**, 277–290, February (2A), 1935.

[6] Hofmann, W.: Furuncles of Face. Arch. f. klin. Chir., **123**, 51, March 15, 1923.

[7] Koslin, I. I.: Primary Staphylococcus Infections of Nose, Lips and Face. ANNALS OF SURGERY, **94**, 7–14, July, 1931.

[8] Ludlow, H.: On Carbuncular Inflammation of Lips and Other Parts of Face. Med. Times, **5**, 287–290, September 18, 1852; 332–334, October 2, 1852.

[9] Martin, W.: The Fatal Outcome of Certain Cases of Staphylococcus Infections of the Face and Lips. ANNALS OF SURGERY, **76**, 13–27, July, 1922.

[10] Powell, L. S.: Septic Thrombosis of Cavernous Sinus; Report of Two Cases. Ann. Otol., Rhin. & Laryngol., **37**, 909–921, September, 1928.

[11] Price, J. W.: Treatment of Infections of Face. ANNALS OF SURGERY, **85**, 329–332, March, 1927.

[12] Roeder, C. A.: Ligation of Angular Vein in Infections of Upper Lip. J.A.M.A., **90**, 272–273, January 29, 1928.

[13] Stout, B. F.: Septic Cavernous Sinus Thrombosis. Report of Two Cases with Recovery of One Following Bacteriophage Therapy. J. Lab. & Clin. Med., **17**, 28–39, October, 1931.

[14] Totten, H. P.: Treatment of Carbuncles of Face. West. J. Surg. Obst. & Gynec., **43**, 609–617, November, 1935.

[15] Treves, F.: Surgical Applied Anatomy, 8th ed., revised by C. C. Choyce. Lea & Febiger, Philadelphia and New York, 1927.

[16] Wheeler, W. I. deC.: Danger of Sepsis About Lips. Surg., Gynec. & Obstet., **43**, 535–537, October, 1926 (editorial).

[17] Wright, V. M. W.: Infections in Dangerous Circle of Face. S. Clin. North America, **12**, 1567–1577, December, 1932.

RIEDEL'S STRUMA AND STRUMA LYMPHOMATOSA (HASHIMOTO)

A COMPARATIVE STUDY

JOHN C. MCCLINTOCK, M.D., AND ARTHUR W. WRIGHT, M.D.
ALBANY, N. Y.

FROM THE DEPARTMENTS OF SURGERY OF THE ALBANY HOSPITAL AND ST. PETER'S HOSPITAL, AND THE DEPARTMENT OF PATHOLOGY, ALBANY MEDICAL COLLEGE, UNION UNIVERSITY, ALBANY, N. Y.

THE present rather generally accepted opinion that struma lymphomatosa (Hashimoto[1]) and Riedel's[2] struma are different manifestations of the same disease process, seems to have originated from a statement made by Ewing,[3] in 1922. As a result of the acceptance of this concept there have been very few investigators who have carefully analyzed these two conditions in an attempt to differentiate them. It is found, therefore, in reading published reports, that many cases in which the clinical and pathologic findings are quite characteristic of struma lymphomatosa are reported as Riedel's struma. From our studies we are convinced that the two conditions are separate diseases and the evidence here presented will, we hope, stimulate a more critical study of them to the end that their etiology and clinical course may be more thoroughly understood.

The clinical differences between Riedel's struma and struma lymphomatosa were emphasized by Graham,[4] in 1931, when he revived Hashimoto's original contention that the two diseases were separate entities. Lee,[5] in his review of the literature, agrees with this concept of Graham's to the extent that he separates the fibrous type from the lymphoid type of pathologic change. Lee, however, in his review, covered the same records that Graham did but in addition included the cases reported after 1931. To prevent confusing duplication in the recording of cases, we have reviewed the literature since 1930 and here record only those cases not included by Graham. Thus, we feel we have available in Graham's report and in this contribution, an account of nearly every case reported as Riedel's struma, chronic thyroiditis, ligneous thyroiditis and struma lymphomatosa. It is surprising that only 60 cases fulfill the clinical and pathologic requirements of Riedel's struma; and only 50 present the findings characteristic of struma lymphomatosa (Hashimoto). In the group we have designated as atrophy and fibrosis (Group III) are 22 cases, in 19 of which there were found foreign body giant cells. It is unfortunate that 80 cases are not available for study and accurate classification, because of insufficient data (Table I).

The literature from 1930 to date contains many incomplete reports. There were found at least 12 original articles reporting a total of 69 cases in all of which inadequate clinical and pathologic information was given.

Submitted for publication December 10, 1936.

The statement made by Ewing, namely, that "the two lesions are different manifestations of the same disease process" has been taken too much for granted and has led many workers to report cases with inadequate clinical

TABLE I

CASES REPORTED SINCE 1931

Author	Reported As	Author's Classification Group I	Group II	Group III	Group IV
Vogel[23]	Riedel's struma	2			
Bothe[24]	Early Riedel's struma		1		
Crane[25]	Chronic thyroiditis				28
Bruce[26]	Riedel's tumor	1			
Kreuzbauer[27]	Chronic thyroiditis				1
Kreuzbauer[28]	Chronic thyroiditis	2		2	1
Prati[29]	Riedel's struma	2			
Traum[30]	Riedel's struma				1
Diez[31]	Riedel's struma	2			
Nestmann[32]	Chronic thyroiditis			1	
Oehler[33]	Eisenharte struma			1	
White[34]	Riedel's thyroiditis		1		
Angerer[35]	Eisenharte struma			Acute thyroiditis	
Melina[36]	Riedel's struma	1			
Nordland and Larson[37]	Thyroiditis				1
Eisen[38]	Riedel's struma				7
Howard[39]	Struma lymphomatosa		2		
Lester[40]	Riedel's struma		1		
Polowe[41]	Struma lymphomatosa				1
Seed[42]	Riedel's struma				5
Benson[43]	Riedel's struma			1	
Emerson[44]	Struma lymphomatosa		1		
Gilchrist[45]	Chronic thyroiditis	1			
Mallory[46]	Struma lymphomatosa		1		
Boyden, *et al.*[6]	Riedel's struma	2	1		6
Roulet[21]	Riedel's struma	2		1	
Poer, *et al.*[19]	Struma lymphomatosa		1		
Tearnan[8]	Riedel's struma		1	1	
Lee[5]	Chronic thyroiditis		3	8	
Clute, *et al.*[14]	Struma lymphomatosa		9		
Clute and Lahey[10]	Thyroiditis				17
Graham[4]	Collected	41	24	3	11
McClintock and Wright		4	4	4	
Totals		60	50	22	79

Group I represents Riedel's struma; Group II struma lymphomatosa (Hashimoto); Group III atrophy and fibrosis with foreign body giant cells; and Group IV cases with insufficient information to permit classification.

and pathologic data and without a careful analysis of all available facts. Likewise the statement of Boyden, Coller and Bugher,[6]—who not only agree with the unitarian concept of Ewing but go even farther and say,

"We do not believe that the process is a distinct entity"—cannot help but imperil a critical study of cases of these diseases. In spite of the many writers who have accepted without question the belief of Ewing, there is a growing number who feel the clinical and pathologic changes observed in each of the two types are such as to make the two diseases separate. It is the sincere hope of the authors that future contributors to this discussion will include complete records of each case in order that students of the subject will not be deprived of any opportunity to study these rare lesions.

TABLE II

SUMMARY OF CASES OF RIEDEL'S TYPE

		Literature	Graham	Author	Average
Sex	Male	14.2%	41.5%	.....	18.2%
	Female	86.8%	58.5%	100%	81.8%
Age	Youngest	24 yrs.	23 yrs.	31 yrs.	
	Oldest	78 yrs.	64 yrs.	53 yrs.	
	Average	43.1 yrs.	36.2 yrs.	41.6 yrs.	40.3 yrs.
Duration of symptoms	Shortest	2 mos.	15 days	14 days	
	Longest	2 yrs.	2 yrs.	2 yrs.	
	Average	9.2 mos.	7.3 mos.	6 mos.	7.5 mos.
Duration of goiter	Shortest	5 mos.	30 days	14 days	
	Longest	23 yrs.	3 yrs.	8 yrs.	
	Average	7.8 yrs.	1 yr.	1.5 yrs.	3.5 yrs.
Thyroid involvement	Unilateral		48.6%	12.5%	
	Bilateral		51.4%	87.5%	69.5%
Hypothyroid	Postoperative.		19%	35%	27%
Number of cases		15	41	4	60

TABLE III

SUMMARY OF CASES OF STRUMA LYMPHOMATOSA (HASHIMOTO TYPE)

		Literature	Graham	Author	Average
Sex	Male	.....	4.2%	.....	1.4%
	Female	100%	96.8%	100%	98.6%
Age	Youngest	26 yrs.	40 yrs.	35 yrs.	
	Oldest	62 yrs.	75 yrs.	53 yrs.	
	Average	50.8 yrs.	52.4 yrs.	44.4 yrs.	49.2 yrs.
Duration of symptoms	Shortest	2 mos.	30 days	1 yr.	
	Longest	36 yrs.	6 yrs.	3 yrs.	
	Average	11.5 mos.	1.2 yrs.	2 yrs.	1.3 yrs.
Duration of goiter	Shortest	2 mos.	3 days	4 yrs.	
	Longest	15 yrs.	6 yrs.	16 yrs.	
	Average	3.8 yrs.	1.3 yrs.	7.5 yrs.	4.2 yrs.
Thyroid involvement	Unilateral				
	Bilateral	100%	100%	100%	100%
Hypothyroid postoperative		77.7%	58%	100%	78.8%
Number of cases		19	24	4	47

As a result of the studies of Graham and the observations made by ourselves, certain clinical differences are apparent. These may be summarized briefly here, and are presented in tabular form in Tables II and III.

Sex.—Sex plays little or no rôle in Riedel's struma; the ratio of female to male is nearly that found in all other types of goiter. In struma lymphomatosa (Hashimoto), however, more than 95 per cent of the patients were women.

Age.—Differences in age are present but are not always of significance in individual cases. In general, however, the average age of patients with Riedel's struma is younger than the average age of those who suffer from struma lymphomatosa. In a series of 60 cases of Riedel's struma the average age of patients was 40, while in 50 cases of struma lymphomatosa the average age was 49.

Duration of Symptoms.—In Riedel's struma the average duration of symptoms was approximately seven months while goiter had been present for an average period of 3.5 years. In struma lymphomatosa the symptoms have usually been present for a somewhat longer period, an average of 16 months with the average duration of goiter slightly over four years.

Thyroid Involvement.—In the case of Riedel's struma the lesion is not always bilateral, approximately 30 per cent of the cases exhibiting involvement of one lobe only. Of the 50 reported cases of struma lymphomatosa, however, all have been said to show involvement of both lobes of the gland.

Hypothyroidism.—Approximately 26 per cent of the patients with Riedel's struma develop hypothyroidism postoperatively while more than three-fourths of those suffering from struma lymphomatosa have definitely diminished thyroid activity after removal of the gland.

In the group which we have designated as atrophy and fibrosis are four cases in which the clinical and pathologic findings are somewhat different from the others. These cases (Nos. 1, 2, 3 and 4) are characterized by inflammatory fibrosis of the gland with the presence of many foreign body giant cells. At least 15 of the cases reported from the literature show similar findings. Clinically, the symptoms referable to thyroid involvement come on fairly rapidly and usually follow acute upper respiratory infections. There may be associated fever as well as pain and tenderness localized over the gland. Although included in this series with cases of Riedel's struma, this group seems to be of a slightly different character and, as pointed out to us by Graham,[7] it is not at all unlikely that further study of the lesion will show it to be a separate form of chronic thyroiditis.

In origin Riedel's struma and struma lymphomatosa show a marked etiologic difference. The former is conceded to be essentially a lesion of inflammatory nature. In most of our cases, as well as in some of those previously reported,[8, 9] a history of acute upper respiratory or dental infection is given as occurring just before the onset of the symptoms of thyroid disease. Clute and Lahey[10] also report a group of 21 cases of Riedel's

struma, in a number of which an acute inflammatory condition of the throat, tonsil, or teeth preceded the onset of the disease.

The mechanism of producing an inflammatory lesion in the thyroid gland, normally so resistant to infection, remains obscure. There is a well marked agreement among students of the subject that the cause is not syphilis or tuberculosis. Smith and Clute[11] report negative bacterial cultures and animal inoculation experiments with tissue from Riedel's struma, yet they still favor a chronic inflammatory process of unknown origin as the cause of the thyroid change. The microscopic picture of extensive fibrosis is in keeping with such a theory of origin. Bohan[12] has reported the isolation from dental infections of organisms which, when injected into a rabbit, produced lesions in the thyroid and thymus glands. Searls and Bartlett[13] isolated identical organisms from the thyroid gland and throat of a patient with acute thyroiditis. Such reports as these, however, are too few and too uncertain to be conclusive and for the present it seems best simply to accept the hypothesis that the lesion is inflammatory in type but of unknown etiology.

The causative factors in Hashimoto's lesion are even more obscure than are those of Riedel's struma. Recently Clute, Eckerson and Warren[14] have indicated that they are of the opinion that struma lymphomatosa is a degenerative change without evidence of an acute inflammatory process. Clute and Warren[15] further imply a difference between Riedel's struma and struma lymphomatosa when they accord separate places to these lesions in the differential diagnosis of thyroid cancer. No explanation has yet been advanced to account for an inflammatory reaction causing in one case marked sclerosis, and in the other hyperplasia of the lymphoid elements. The lymphadenoid type of thyroid has been described by Williamson and Pearse[16] as being a physiologically subnormal gland undergoing a compensatory lymphoid hyperplasia with the lymphocyte reaction proportional to the failure of the usual epithelial hyperplastic effort. Such a process would necessarily be a diffuse one, and indeed struma lymphomatosa of Hashimoto is generally of this character. Exhaustion atrophy is a recognized pathologic change in Hashimoto's lesion and this degenerative process might well be associated with some form of compensatory hyperplasia, as Williamson and Pearse suggest.

McCarrison,[17] by the use of a deficient diet, has produced experimentally a thyroid lesion which is remarkably like that of struma lymphomatosa. Dietary deficiency should also, if a part of the etiology of this lesion, produce changes in other organs. The report by Shaw and Smith[18] of a case of struma lymphomatosa in which there were adrenal lesions similar to those in the thyroid gland, as well as enlargement of the thymus, seems to indicate a causative factor of generalized character. Graham first enunciated the theory of the systemic nature of Hashimoto's lesion and although there is yet only meager proof of its truth, the concept that the changes in the

thyroid gland are only a local manifestation of a generalized disease seems to be compatible with the clinical course of struma lymphomatosa.

The history and the direct examination of the patient are of greatest importance in making a differential diagnosis between Riedel's struma and struma lymphomatosa. On palpation, tenderness and the presence of a very hard, fixed, resistant gland are strongly indicative of Riedel's struma. So hard does the gland feel on palpation that it is commonly mistaken for malignant disease. The smooth, diffuse hardness should suggest benign struma when contrasted with the irregular nodularity of neoplasm. This hardness of the gland in Riedel's struma is usually much more marked than the resilient firmness of struma lymphomatosa. Each of the lesions may cause dyspnea and dysphagia with a feeling of constriction or tightness around the neck. Weakness and fatigability may likewise be common to both, although the last two symptoms are more frequent with struma lymphomatosa.

Patients with struma lymphomatosa require a long time to return to normal, if they do at all. Their usual course is progressive hypothyroidism associated with such symptoms as fatigability, generalized weakness, and sometimes gastro-intestinal disturbances. On the other hand, those patients with Riedel's struma, following surgical treatment, tend to improve quite rapidly and frequently return to normal.

A clinical diagnosis of either of the two conditions is seldom made. There are no pathognomonic signs or symptoms in these cases and it is only by putting together all possible findings, past and present, objective and subjective, that a clinical hint may be obtained as to what is the true nature of the lesion. The age of the patient, antecedent history of upper respiratory or dental infection, degree of hardness and fixity, and the amount of gland involved, must all be carefully considered. Riedel's struma gives rise to the greatest difficulty in the clinical identification. The number of cases in which a diagnosis of carcinoma is made in cases of this disease is very high, while malignant disease is usually not suspected in the Hashimoto type of change. If the diagnosis is not made when the patient is examined clinically or by direct observation and palpation at the time of operation, rapid frozen section examination of the tissue may often be more confusing than helpful. We are, therefore, opposed to the making of such inadequate rapid studies of thyroid tissue. The most dependable findings are, we think, an accurate history, properly evaluated, and careful clinical examination of the gland.

Heretofore attention has been drawn to the clinical differences between these two lesions. However, from the standpoint of the morphology of the gland itself, there are also significant differential features which should be mentioned. Grossly the gland in Riedel's struma is very firm, usually stony hard, with extreme diffuse fibrosis. There is loss of lobulations and the incised surfaces of the gland show little evidence of the typical colloid-containing acini which characterize the normal structure.

In the case of struma lymphomatosa, on the other hand, the tissues are

firm but not hard, smoothly lobulated, and are not markedly fibrosed. The normal lobular character of the gland is still present although on section there is found definite diminution or almost complete absence of colloid material. Often the appearance of the gland resembles that of an enlarged, firm lymph node.

Histologically, too, the glands of the two diseases differ from each other. Riedel's struma is characterized by marked diffuse sclerosis of the affected portions of the gland, with varying numbers of persisting acini. Where the acini do persist, they are grouped together in small nests or clusters and appear compressed by the surrounding dense fibrous stroma. Such groups of acini apparently indicate where a lobule at one time existed. The cells of these persistent glands are not remarkable. In general they resemble those which form the normal acini. Accumulations of lymphocytes, and occasionally of other leukocytes, are often found, but these accumulations are focal in distribution and appear to be definitely of inflammatory nature. Lymph nodules are not often found.

In contrast, struma lymphomatosa, while it shows some evidence of fibrosis, is characterized chiefly by marked, often extreme, lymphoid infiltration of the gland. This infiltration is most marked in the interacinar tissues and is often associated with a peculiar, but quite typical atrophy of the neighboring acini, which tend, sometimes, to be packed closely together, sometimes to be separated from each other by lymphocytes. The cells which form many of these atrophic acini are large, parenchymatous, acidophilic, with more cytoplasm than normal and small hyperchromatic nuclei. They appear degenerated rather than normal. Colloid is diminished in amount and is often absent. Large hyperplastic lymph nodules are commonly present. These are sometimes so large that they may be recognized by the unaided eye. The lymphoid infiltration is not associated with other inflammatory cells and does not resemble that which occurs in the gland of toxic goiter after iodine treatment. The glandular stroma is not inflamed in the ordinary sense, but often appears to be actually converted into typical lymphoid tissue, which lends support to the view that the change is not primarily inflammatory, but is rather, as Williamson and Pearse have suggested, the result of hypoactivity on the part of the epithelial elements.

Even though conclusive evidence is lacking, we feel that the clinical and pathologic differences herein described warrant placing the two lesions into distinct groups. Future studies in the differentiation of the diseases, with careful recording of characteristic points observed in each lesion, will lead to better understanding of these conditions and eventually to accurate classification.

CASE REPORTS

Case 1.—Mrs. E. H., age 32, experienced pain in the neck, anteriorly, then on both sides, two and one-half months before her admission to the Albany Hospital May 27, 1930.

There had been slight fever, some dysphagia but no dyspnea. Her appetite was poor and she had lost 12 pounds in weight. Moderate increase in nervousness and fatigability had been noted.

The thyroid gland was bilaterally enlarged, being almost twice normal size. It was slightly tender and very hard. The remainder of the examination was without bearing on the thyroid problem. The blood pressure was 120/80. The clinical diagnosis was thyroiditis.

At operation the right and left lobes were found to be extremely hard and fibrous in character, particularly on the outer sides. The inner aspects of the lobes were more nearly normal in appearance. Portions of tissue were removed from each lobe.

The excised tissue was firm, hemorrhagic and glandular. On section it appeared tough and slightly edematous. Microscopically, sections from this gland showed large foci of diffuse fibrosis which involved chiefly the interlobular stroma. So abundant was the fibrous tissue that it separated and compressed the acini, causing them to appear as small atrophic gland-like spaces embedded in a dense collagenous matrix. The stroma contained moderate numbers of small arterioles and venules which were not congested. Most of the atrophic gland spaces contained colloid. Around many of them colloid had been liberated and was being phagocytized by foreign body giant cells. Here and there, small focal accumulations of lymphocytes were present in the stroma, but there was no general, diffuse lymphocytic infiltration. In a few places suggestive lymph nodule formation was noted.

The epithelial cells of the atrophied acini were small, low cuboidal or flat, pale staining, finely granular and contained large oval nuclei. Cytoplasmic granules were much less abundant in these epithelial cells than in those of the struma lymphomatosa type. Different sections from the same gland showed a varying amount of fibrosis from only a slight increase in the fibrous stroma around the lobules to the more extensive changes described above. Acini seen in the less dense stroma showed little deviation from normal. The changes in this gland were those of chronic thyroiditis with diffuse interacinar fibrosis, possibly an early stage of Riedel's stroma.

The patient was observed at intervals until February, 1932, at which time she was well, had no complaints, but was compelled to take thyroid extract, one-half grain twice daily.

Case 2.—Mrs. G. C., age 47, was admitted to the Albany Hospital January 28, 1930. Four weeks before her entrance she had had sore throat and a cold which were followed in one week by soreness in the neck and increase in the size of the thyroid gland. There had been pain of moderate severity in the enlarged gland, slight fever, anorexia and a general feeling of tiredness. Ten pounds were lost during the present illness. Occasionally in the past she had had sore throats and during childhood, scarlet fever.

Examination of the patient showed little except for the bilaterally enlarged thyroid gland that was stony hard and fixed to the trachea and surrounding structures. The blood pressure was 130/68. A clinical diagnosis of Riedel's struma was made.

Operation revealed adherence of the periglandular muscles to the capsule of the thyroid gland. The gland was stony hard, smooth and enlarged three times normal size. Wedges of tissue removed from each lobe and the isthmus were fibrous in appearance and seemed to contain very little thyroid tissue.

Sections from the gland revealed diffuse sclerosis with almost complete loss of the acini. The scar tissue was dense, hyaline and focally infiltrated with lymphocytes. Here and there, small numbers of atrophic acini which contained little or no colloid were found. The epithelial cells lining these acini were cuboidal with finely granular cytoplasm and large hyperchromatic nuclei. In some situations there were larger, more readily recognizable acini, the lining epithelium of which was almost identical with that of the normal thyroid acinus. Colloid within these latter acini

was fairly abundant. Often the colloid was infiltrated with phagocytic endothelial leukocytes and scattered diffusely throughout the dense fibrous tissue were varying numbers of foreign body giant cells about masses of colloid. Histologically the findings were those of marked thyroiditis with diffuse fibrosis, not unlike Riedel's struma.

This patient was followed clinically for 11 months. She remained perfectly well and required no medication.

Case 3.—Mrs. E. D., age 31, entered the Albany Hospital July 21, 1930, because of soreness and tenderness in her neck. This illness began six weeks before her admission and had been treated by hot applications. Four weeks before entrance a lump was noted in the middle of the neck which slowly increased in size. Slight fever, dyspnea, anorexia and a loss of 15 pounds in weight were associated symptoms. For

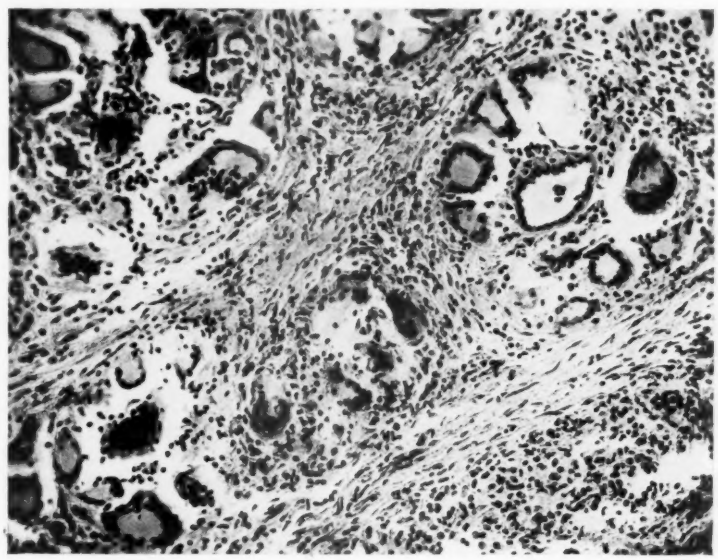


FIG. 1.—(Case 3.) Chronic thyroiditis with foreign body giant cells (×200).

about two months the patient had noticed that she became more easily fatigued than normal. For years the patient had suffered from tonsillitis and head colds.

The thyroid gland was hard, tender, diffusely enlarged to almost three times normal size, but the overlying skin and tissues showed no evidence of any inflammatory process. The blood pressure was 108/60. The clinical diagnosis was thyroiditis.

At operation the preglandular muscles were found to be adherent to the capsule of a very hard thyroid gland. Small pieces of tissue were removed from each lobe. Grossly these fragments consisted of dense, rubbery, yellowish-white, unrecognizable tissue with white fibrous bands running through it. Acini were not visible.

Sections from this gland showed it to be densely and diffusely sclerosed, the sclerosis being both interacinar and interlobular, but the lobules were still distinctly visible and appeared as scarred areas in which small to moderate numbers of atrophic acini were present. In some of the lobules no acini were recognizable, in others minute, contracted, compressed, gland-like spaces were embedded in dense stroma. These spaces were lined by small pale-staining, cuboidal cells with slightly granular cytoplasm and large hyperchromatic nuclei. In still other situations readily recognizable but irregularly sclerosed thyroid tissue was visible. The acini in these situations were lined by flat epithelial cells not unlike those of the normal thyroid gland. Separating all of the lobules, whether they contained glands or not, were dense, broad, almost acellular bands

of hyaline collagenous tissue in which small numbers of blood vessels were present. In practically all of the lobules, from one to many foreign body giant cells, which appeared to be phagocytizing colloid were found (Fig. 1).

The histologic changes were those of marked chronic fibrosing thyroiditis of the type described by Riedel and with an associated foreign body giant cell reaction.

The patient was last seen in August, 1936, at which time she was well and required no medication.

Case 4.—Mrs. F., age 48, was admitted to the Albany Hospital, October 8, 1935. Two months before admission there had been a traumatic hyperextension of the neck followed in a few days by an upper respiratory infection and coincident pain in the region of the thyroid gland. Chills and fever were present at the onset, but the acute symptoms rapidly subsided, leaving only soreness. There had been a weight loss of nine pounds. One month before admission a small swelling was noted in the region of the thyroid gland.

The general examination was not remarkable but locally there was found a bilaterally enlarged thyroid gland that was extremely hard to palpation. The right lobe was the size of a lemon and the left was slightly smaller. The gland was firmly fixed to the deeper structures of the neck. The blood pressure was 150/90. The clinical diagnosis was possible malignancy.

At operation the overlying muscles and the deeper structures, including the trachea, were found to be adherent to the capsule of the gland. At the left inferior pole were two small adenomata, one of which was cystic, but the rest of the lobe showed the same changes as were found throughout the other portions of the gland. Subtotal thyroidectomy was performed with noticeably little bleeding. The cut surfaces of the gland were grayish-white in color, tough and firm in consistency, and fibrous in appearance.

The sections showed diffusely and markedly sclerosed thyroid tissue. In some areas normal sized or slightly enlarged, colloid-containing acini were found while in other situations the recognizable acini were sclerosed and atrophied. Throughout the sections dense fibrous tissue was found, often containing giant cells grouped about colloid material in pseudotubercle formation. Large foci of lymphocytic infiltration were seen but active germinal centers were not present. There was no histologic evidence of malignancy in any of the sections. The changes were characteristic of Riedel's struma, with a foreign body giant cell reaction.

This patient is still being followed and when last seen in June, 1936, was well and required no medication.

Case 5.—Mrs. G. C., age 53, had noted a swelling in the anterior part of her neck, only two weeks before admission to the Albany Hospital, September 23, 1929. Mild dyspnea, general weakness, and a weight loss of five pounds characterized the present illness.

This patient had had typhoid fever in 1914, an hysterectomy in the same year, and a left mastectomy in 1919 for a benign tumor. Chronic nasal infection had been present for six months prior to admission.

The thyroid gland was enlarged and contained firm nodular masses in the right lobe and isthmus. The cervical lymph nodes were just palpable but were not tender. The remainder of the examination was not remarkable. The blood pressure was 118/70. The clinical diagnosis was chronic thyroiditis.

The gross specimen consisted of dense, hemorrhagic fibrous tissue which did not resemble thyroid gland. Microscopically there was marked diffuse interacinar and interlobular fibrosis of the entire gland with reduction in size of the lobules and atrophy and disappearance of great numbers of the acini. The acini which remained were contracted and atrophic, and were lined by flat or low cuboidal epithelial cells. These were pale-staining and contained finely granular cytoplasm and oval nuclei in which

were small amounts of chromatin. Many of the acini contained small amounts of colloid. In other parts no acini at all were present and the lobule remained as a small sclerosed focus, infiltrated with focal collections of lymphocytes and plasma cells, the former predominating. No typical lymph nodules were present. The interlobular stroma was abundant, very dense and almost acellular and contained moderate numbers of rather thick-walled, contracted blood vessels. The histologic changes were those of early Riedel's struma.

The postoperative course was uneventful. She was seen at intervals until July, 1931, at which time she was entirely well and required no medication. In August, 1936, she was requested to report for a check-up examination, and was found to be free from symptoms.

Case 6.—Mrs. N. B., age 45, was admitted to the Albany Hospital, October 16, 1931, complaining of swelling and tenderness of the neck. Six months previously she began to experience a sensation of tightness and pain in the neck which gradually became associated with dyspnea and dysphagia. Increased emotional instability and nervousness were described by the patient as a "nervous breakdown." In a two-month period the patient lost 21 pounds, after which her symptoms abated and there was marked improvement until two weeks before coming to the hospital, when a tender swelling was discovered in the neck. The blood pressure was 130/80.

A hard, somewhat tender thyroid gland, twice normal size, was found. No other abnormality appeared and a clinical diagnosis of chronic thyroiditis was made. At operation several indurated areas were found in both lobes, more especially the left. The gland was adherent to the surrounding structures. The isthmus and a wedge of tissue from the left lobe were removed.

Sections from this gland showed marked diffuse fibrosis with atrophy and diminution in the number of the acini. There still remained traces of the usual lobular arrangement. Within the lobules the stroma was thick, dense, and infiltrated with lymphocytes, plasma cells, and occasional endothelial leukocytes and eosinophils. The stroma about the lobules was markedly increased in amount and in places appeared almost hyaline, but showed less evidence of inflammatory infiltration. In many of the lobules there still remained small numbers of irregular acini that contained no colloid. The epithelial cells lining these acini were small with large oval nuclei and very little cytoplasm. Histologically the picture was that of marked chronic thyroiditis with diffuse fibrosis, an early stage of Riedel's struma.

The patient was compelled to take one-half grain of thyroid extract three times daily for six months, until July, 1932, since which time she has remained well.

Case 7.—Mrs. A. S., age 42, entered the Albany Hospital, April 4, 1925, complaining of a goiter that had been present for eight years. During the year prior to admission there had been a gradual increase in the size of the goiter associated with anorexia, dyspnea and dysphagia, all more marked during the last month. Weight loss during the past year was 11 pounds. She had suffered occasional acute upper respiratory infections. Her mother had suffered from a goiter.

The thyroid was diffusely enlarged, lobulated, firm to stony hard in consistency. The left lobe and isthmus were attached to the trachea and surrounding parts but the right lobe seemed freely movable. No other noteworthy changes were observed in the general examination. The blood pressure was 160/120. The clinical impression was malignant disease of the thyroid gland.

At operation wedges of tissue were removed from each lobe together with the entire isthmus. A portion of the remaining gland tissue was destroyed by cauterization.

Sections from this gland showed large foci of dense hyaline fibrosis in which the collagen was abundant and strongly resembled that found in a keloid. Scattered diffusely throughout the scar tissue were moderate numbers of plasma cells and occasional focal collections of lymphocytes and polymorphonuclear and endothelial leukocytes.

Occasional large accumulations of lymphocytes were found but there were no true lymph nodules. Blood vessels were not abundant. Here and there, atrophied acini were found. These occurred singly or in small groups embedded in the dense stroma (Fig. 2).

In other areas there was little or no evidence of sclerosis of the thyroid tissue. In these regions acini which were lined by flat, often normal appearing epithelium were found. The acini contained varying amounts of colloid which stained poorly, appeared shrunken, and was often vacuolated. Occasionally dilated acini were present. There was no evidence of malignant diseases. The histologic picture was that of ligneous thyroiditis or typical Riedel's struma.

This patient was followed from time to time until August, 1930. She remained

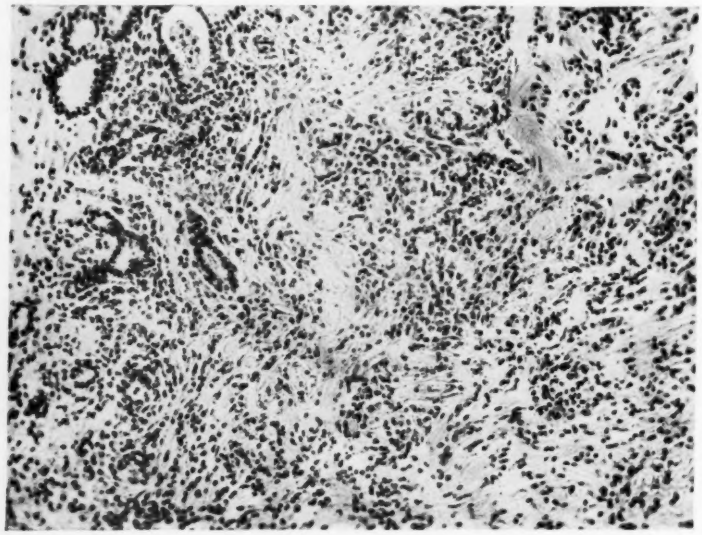


FIG. 2.—(Case 7.) Typical Riedel's struma, showing marked and extensive fibrosis, with compression of the remaining acini (×125).

well, required no medication from the point of view of the thyroid, although the blood pressure remained the same. An answer to our questionnaire in August, 1936, revealed that she was well and free from symptoms.

Case 8.—Sister M. D., age 35, entered St. Peter's Hospital on January 28, 1935, complaining of goiter of three years' duration associated with dyspnea and dysphagia for the past two years. These symptoms had become progressively more severe and were accompanied by choking sensations in the neck and occasional indefinite pains in the throat. Hardness of the goiter was noted when symptoms first began. At the onset tachycardia, tremor and nervousness were noted but had been absent for six months prior to admission.

Cholecystostomy and appendicectomy were performed in 1929; cholecystectomy in 1931, and tonsillectomy in 1932. The patient suffered from frequent sore throats before the removal of the tonsils.

The thyroid gland was bilaterally enlarged and slightly lobulated with rather a sharp margin on the left side. The gland was firmly fixed and stony hard in consistency. There was no cervical lymphadenopathy. Laboratory studies were negative. Roentgenologic examination of the chest showed no evidence of tumor metastases. A clinical diagnosis of Riedel's struma was made. The blood pressure was 124/80.

Careful dissection at operation was necessary in order to free the muscles which were adherent to the gland. The right lobe and isthmus were entirely involved in

the change but the left lobe appeared normal in its posterior two-thirds. The isthmus was excised and wedges of tissue were removed from each lobe with destruction of a part of the remaining tissue with the cautery. There was remarkably little bleeding from the gland substance. The tissue excised was whitish in color, hard, and fibrous, with only here and there a suggestion of cellularity.

Sections from this gland showed it to be composed almost entirely of dense fibrous tissue which was diffusely but only moderately infiltrated with lymphocytes and plasma cells. Only rare evidence of lobulation persisted and the dense, finely fibrillar collagenous tissue resembled that of a keloid. Between the dense strands was a more delicate fibrous meshwork throughout which inflammatory cells, chiefly lymphocytes, were diffusely scattered. In places these cells were collected in large foci but nowhere were typical lymph nodules found.

The acini were almost entirely missing, only a few round or oval glands being found in one portion of one section. In general, these remaining acini were small, compressed, and lined by cuboidal epithelial cells which were often heaped up into a double layer due to crowding. The cytoplasm of these cells was pale-staining and contained small pinkish granules. The nuclei were oval and stained rather diffusely but were not hyperchromatic. In most of the acini colloid was absent, but in some there was a small accumulation of pink-staining, often abnormal appearing colloid.

The arterioles of the gland appeared to be actually reduced in number since sclerosed and obliterated vessels were occasionally observed. Those arterioles that persisted were thick walled and markedly contracted and were not infrequently surrounded by small numbers of lymphocytes.

Very careful examination was made for evidence of malignancy but no atypical cells or gland-like structures could be found in any part of the sections. Histologically, therefore, the condition was that of Riedel's struma.

A diagnosis of scirrhous carcinoma was made at the time of operation from a study of frozen sections of the gland. An even more pertinent fact was that subsequent study of sections of this gland by five pathologists resulted in two diagnosis of carcinoma, two of Riedel's struma and one of a benign lesion probably Riedel's struma, but with malignancy not positively ruled out. The patient, however, remained well, and over a year after operation there was no evidence of local or distant recurrence, although the undestroyed portion of the gland could still be palpated.

Case 9.—Mrs. L. G., age 38 years, entered the Albany Hospital, May 18, 1933. A mass had been present in her neck for seven years. It had appeared first following the birth of her first child. The size of the mass varied but seemed to decrease somewhat until the second pregnancy three years later when it again grew larger. At that time the patient noticed that she became fatigued easily. The basal metabolic rate was minus two. A spontaneous recovery followed. After the third pregnancy two years before admission the gland again became enlarged and continued to increase slowly in size. Again unusual fatigability was an early symptom and this became more severe during the four months preceding her admission to the hospital. During the last two months of her illness there had also been dyspnea and a sense of substernal pressure. There was no loss in weight. At the age of 22 this patient had had scarlet fever and during 1918 suffered from influenza. Several relatives on her father's side of the family had had goiters.

The thyroid gland was bilaterally enlarged. The right lobe was of nearly normal consistency but the left was irregular and very firm to the examining fingers. The blood pressure was 100/60. The remainder of the examination was within normal limits. The clinical diagnosis was nontoxic diffuse goiter.

At operation, the right and left lobes were of about equal size, measuring 7.5 by 5 by 5 cm. A pyramidal lobe was present. A subtotal thyroidectomy was performed.

The most noteworthy histologic changes were the extremely marked lymphoid infiltration of the stroma and the great reduction in size of the thyroid acini. The

latter structures were small, contracted, irregular in shape. They contained little or no colloid. Their epithelial lining was composed of medium sized to large, parenchymatous, cuboidal cells, with much cytoplasm and distinct, often hyperchromatic, nuclei. Often small groups of acini were embedded, like small islands, in the dense lymphoid stroma. In many places actual lymph nodule formation was observed. Some of the nodules were minute while others were very large and contained active germinal centers. The gland was divided into indefinite lobules by thin but dense strands of hyaline connective tissue (Figs. 3 and 4). These changes were present in practically all of the lobules. The only noticeable exception was a moderately hyperplastic papillary cystadenoma which was present in one section. This apparently benign tumor was completely surrounded by lymphocyte-invaded stroma. Blood vessels of the gland were not abundant and showed only slight evidence of hyperemia. The histologic changes were those of marked struma lymphomatosa (Hashimoto). Dr. Allen Graham, pathologist to the Cleveland Clinic, concurred in this diagnosis.

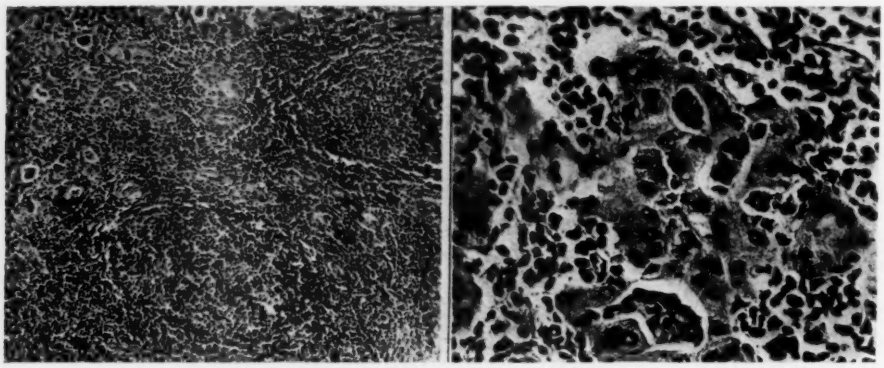


FIG. 3.—(Case 9.) Typical struma lymphomatosa showing lymph nodules, diffuse lymphoid infiltration, and the large parenchymatous acinar cells (×130).

FIG. 4.—(Case 9.) High power of Fig. 3 showing more clearly the typical acinar cells surrounded by diffuse lymphoid infiltration (×400).

After operation the basal metabolic rate was minus 18, but the patient remained symptom free until November, 1933, when the first evidence of clinical hypothyroidism appeared. The basal metabolic rate at this time was minus 30 and thyroid extract was given, one grain twice daily. This medication has been continued and increased from time to time until now, July, 1936, the patient is taking four grains daily.

Case 10.—Mrs. M. T., age 53, was first admitted to the Albany Hospital, March 31, 1929, for a goiter which had been present for 16 years but that had been producing symptoms only during the preceding three years. The principal symptoms were occasional periods of tachycardia associated with a feeling that the heart sometimes skipped beats. For three years the patient had become fatigued unusually easily. Dyspnea on exertion and periods of mental depression had been troublesome during the six months immediately preceding her admission. Throughout the present illness a sense of tightness in the neck, as if a rope were tied about it, had been experienced.

The patient had had three previous operations, hysterectomy, appendicectomy and herniorrhaphy. During childhood she had suffered from diphtheria and scarlet fever.

The right lobe of the thyroid gland was enlarged to the size of a lemon and was hard to palpation. The left lobe was also enlarged, but was nodular and of softer consistency than the right. The remainder of the examination was without note. The blood pressure was 145/90. The preoperative diagnosis was probable carcinoma.

The right lobe at operation was hard, nodular, vascular, and was subtotally resected. The blood supply to the left lobe was ligated without removal of tissue. Grossly

the excised tissue was grayish-red and nodular on its external surface. The cut surface was irregularly lobulated and yellowish-gray in color, fibrous in appearance and showed little colloid. The process was diffuse throughout the gland.

Sections from this gland showed marked diffuse infiltration of the stroma with lymphocytes. These cells varied in number in different places, in some situations occurring in great numbers and being packed between and around atrophic acini; in others being less abundant and appearing as loose accumulations in the interstitial tissue. Here and there, typical lymph nodules were present. The acini were greatly reduced in size but for the most part were composed of large, pale-staining, acidophilic cells in the centers of which were large oval nuclei with varying amounts of chromatin. The majority of the atrophied acini contained small amounts of colloid which were not infrequently infiltrated with phagocytic cells. The epithelial cells showed no evidence of multiplication and were not neoplastic in type. The blood vessels were not unduly

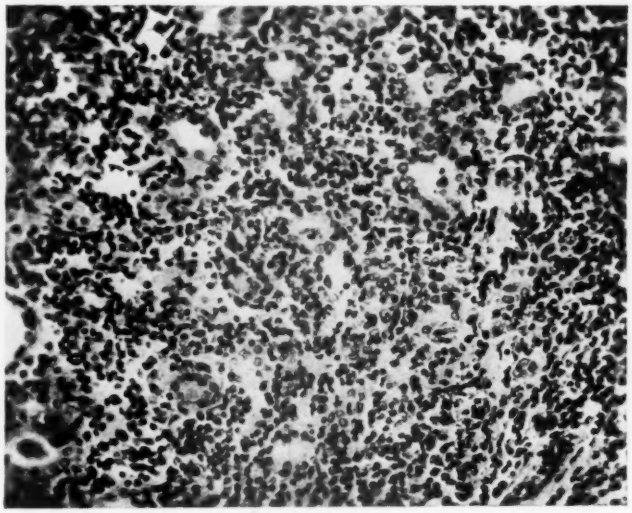


FIG. 5.—(Case 10.) Histologic changes seen at the time of the first examination. The changes are characteristic of struma lymphomatosa (×180).

abundant (Fig. 5). Foci of sclerosis were only rarely seen. The changes were those of struma lymphomatosa (Hashimoto).

This same patient was readmitted on April 7, 1931. She had regained her strength, was able to do some of her work, but her neck had never felt normal following the previous operation. Two months before the present admission she had had an acute pharyngitis and laryngitis after which she experienced dyspnea and dysphagia amounting to a sense of strangulation when lying down. Anorexia and recurrence of the weakness were noted. The general examination was no different from that of the first admission. The blood pressure was 130/70. Under the scar of the previous operation the left lobe was palpably enlarged and quite firm.

The left lobe was subtotally resected at operation and exploration of the right lobe revealed thyroid tissue, equal in volume to that of the left, which extended into the substernal region. Each lobe was subtotally resected at this operation. The outer surface of the tissue removed was bluish-gray in color; its consistency, firm to hard. Lobulation was distinctly visible on the cut surfaces which were smooth, glistening, and of reddish-bown color. Very little colloid was present.

Microscopic examination showed changes which strongly resembled those observed two years previously. Foci in which closely packed acini containing very little stroma and rare lymphocyte accumulations alternated with foci in which the stroma

was more abundant, the glands smaller, and lymphocytic infiltration more marked and diffuse. In some situations fibrous tissue was fairly abundant. In foci of the first type, which were less prominent, the acini were normal in size, were lined by flat epithelial cells, and contained colloid. Foci of the second type were more numerous. Their acini were atrophic, were lined by relatively large pale, pink-staining cells with granular cytoplasm and irregular nuclei, and contained small amounts of colloid. While lymphocytic infiltration was diffuse it was still patchy, in some areas surrounding groups of acini while in other situations the infiltration surrounded each acinus. Small numbers of lymph nodules were present. The fibrous tissue was diffusely infiltrated with lymphocytes (Fig. 6). The histologic changes were those of struma lymphomatosa with which there was also a moderate degree of sclerosis.

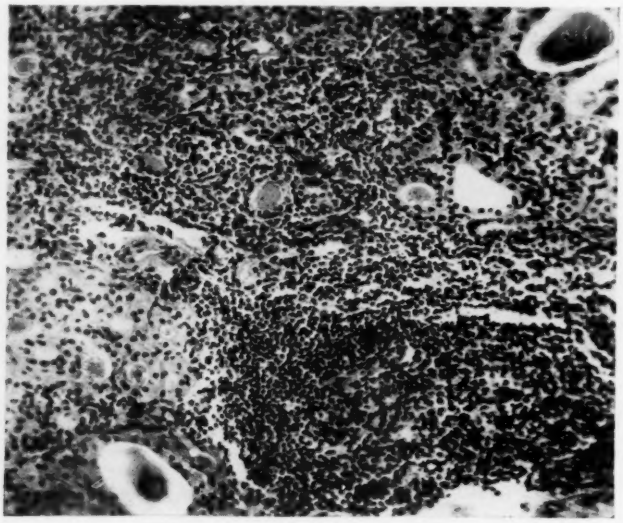


FIG. 6.—(Case 10.) Histologic changes observed at the time of the second examination, two years later. Again, the lymphoid infiltration and changes in the acinar epithelium are characteristic of struma lymphomatosa (×130).

This patient was seen in July, 1936. She stated she had been perfectly well until the Fall of 1935. Since this time she had noted rare choking sensations in the neck. Following an acute upper respiratory infection in December, 1935, she had noted she became tired more easily than before. Both thyroid stumps were palpable, and woody hard, but were apparently not fixed to the overlying structures. The patient was not greatly inconvenienced by these symptoms and was able to do her own work. She had not taken thyroid extract since May, 1934, although her skin was slightly dry and she frequently felt sleepy during the daytime.

Case 11.—Mrs. W., age 51, was admitted to the Albany Hospital, April 17, 1936, complaining of a goiter which had been present four years. During the year preceding admission she had noted pulling sensations in the neck, increased fatigability, and occasional attacks of tachycardia before entrance. There was no history of tremor or of hyperhydrosis. She had had occasional occipital headaches for about two years.

The general physical examination was not remarkable except for a blood pressure of 190/120. There were no eye signs suggestive of hyperthyroidism. The thyroid gland was diffusely enlarged, lobulated, and firm. The preoperative diagnosis was nontoxic nodular goiter.

Operation showed the entire thyroid gland to be enlarged. The glandular tissue was grayish-white in color and had the gross appearance of struma lymphomatosa. The right, left, median and pyramidal lobes were subtotally resected.

The specimen consisted of two masses of thyroid tissue, one 6 by 5 by 2 cm. in size, the other 5 by 3.5 by 2 cm. Each mass was partly covered by a thin, nodular capsule (Fig. 7). On section the tissue was rubbery in consistency, lobulated, and yellowish in color.

Microscopically the sections showed irregular, marked diffuse lymphoid infiltration between many of the acini. In some lobules this infiltration was not pronounced. Moderate numbers of typical lymph nodules with germinal centers were observed. The majority of acini were small and were composed of large cuboidal cells with eosinophilic cytoplasm and centrally placed nuclei. In a few situations the lymphocytic infiltration was so marked that acini were barely visible. There was no evidence of glandular hyperplasia. Colloid, although present, was reduced in amount. The changes were those of struma lymphomatosa.

FIG. 7.—Thyroid gland removed from Case 11. Struma lymphomatosa (Hashimoto).

After operation a basal metabolic rate was plus five. The patient remained well and continued to improve until June 15, 1936, when symptoms of hypothyroidism appeared and thyroid extract, one-half grain a day, was prescribed.

Case 12.—Mrs. M. J., age 55, was admitted to the Albany Hospital, September 22, 1934, for relief of a feeling of pressure which had been present in the neck for two years. During this time the patient had had occasional choking sensations. She had a feeling that a string was tied about her neck. Dyspnea began gradually and was associated with tachycardia on exertion. The patient complained of tiring more easily during her illness than before its onset. The symptoms had been progressively increasing in severity. Blurring of vision had been present on occasions. There was no weight loss. The general physical examination showed little of note except for diffuse enlargement, slight tenderness, and moderate firmness of the thyroid gland. There were no eye signs suggestive of hyperthyroidism. Blood pressure was 170/100. The first impression was nontoxic diffuse goiter.

At operation the right lobe was found to be moderately enlarged, measuring 6 by 3 by 3 cm. in size, while the left lobe was slightly smaller. Both lobes appeared to be the seat of mild colloid goiter. Subtotal thyroidectomy was performed.

Grossly the material consisted of two partially encapsulated lobes of the thyroid gland. On section these were found to be moderately firm with small foci of colloid distention which were separated by areas in which glandular tissue could not be recognized.

Histologically the most significant changes were focal accumulations of lymphocytes in the stroma of the gland, with many large, hyperplastic lymph nodules scattered within the affected foci. Where the lymphocytic infiltration was most marked, the acini were small and shrunken and their epithelial cells were large, moderately acidophilic, and often resembled liver cells. Little or no colloid was present in these acini. Here and there moderate fibrosis was noted. Between these foci of lymphoid hyperplasia and fibrosis, somewhat enlarged acini containing from small to moderate amounts of colloid were present. In these situations lymphocytic infiltration was not present. The histologic changes were those of early struma lymphomatosa (Hashimoto).

This patient was last seen in July, 1936. Since her hospital stay she has steadily improved. Mild cramp-like pain in the muscles of her extremities had caused some discomfort but the blood calcium level has been normal. Up to the present time she has required no thyroid medication.

Discussion.—In the introduction to this paper we called attention to the fact that the majority of students of thyroid disease, accepting the view held by Ewing, have considered that struma lymphomatosa (Hashimoto) and ligneous thyroiditis of Riedel were different stages or manifestations of the same disease. In recent years, however, there has been a tendency away from this unitarian concept since Graham first emphasized certain differential features in the two conditions. Lee and Clute, Eckerson, and Warren, and others now believe that the diseases are separate and distinct. Poer, Davison and Bishop[19] quote Foot as saying, "Hashimoto's struma has no connection with Riedel's struma and they represent two distinct processes—the one an overgrowth of lymphoid tissue followed later by fibrous invasion that may be more a metabolic than an inflammatory process; the other a fibrous overgrowth in response to some inflammatory stimulus."

We agree with those authors who consider struma lymphomatosa (Hashimoto) and Riedel's struma to be separate diseases, and have reviewed 12 personally observed cases. Four of these showed the clinical and pathologic changes characteristic of Riedel's struma; four exhibited a peculiar type of chronic thyroiditis characterized by diffuse fibrosis with foreign body giant cells, a lesion which may at some future time be proven to be a separate entity; and four that presented the changes characteristic of struma lymphomatosa. Although this series of cases is too small a group from which to draw valid conclusions, it is significant, we believe, that our findings in general agree, often strikingly, with those of other investigators who have attempted to separate the two diseases. That definite, though sometimes inconstant, clinical differences exist, is now quite well established.

It is evident, for example, that struma lymphomatosa occurs in an older group of patients, thereby making it difficult to accept the theory that this lesion is the precursor of Riedel's type of change. Symptoms are present over a longer period of time in Hashimoto's lesion than they are in Riedel's

struma, suggesting an etiologic difference. This latter suggestion is emphasized by the slow return to normal in patients with struma lymphomatosa and by the greater number of these cases, as compared with Riedel's struma, that require postoperative medication with thyroid preparations. Struma lymphomatosa, in all reported cases, has been bilateral while Riedel's struma has not been; the former lesion seems to develop in preexisting goiters while the latter is more often the primary change in the gland. The similarity of all these findings in the three series of cases supports the thesis that the two lesions are clinically quite separate and distinct.

Pathologically, too, there are differential features which are apparent to the practiced eye not only in the fresh specimen, but even more markedly, perhaps, in the histologic preparations. In Riedel's struma the changes are inflammatory in character with moderate to extreme fibrosis, excessive hardness of the gland, disappearance of many of the acini and shrinkage of others, and diffuse or focal infiltration with lymphocytes and occasionally other leukocytes. The persistent acini do not vary markedly from normal.

Struma lymphomatosa, on the other hand, is characterized by moderate firmness and irregular lobulation of the gland, extreme lymphoid hyperplasia with lymph nodule formation, and peculiar changes, which appear degenerative, in the epithelial cells of many of the acini. These cellular changes we believe to be significant.

The opportunity of studying one case of struma lymphomatosa at two different periods, the second time after an interval of two years, has been especially enlightening. Heretofore the majority of the reported cases which have been studied more than once have dealt with Riedel's struma. Perman and Wahlgren,[20] for example, report a case studied a second time after an interval of 18 months. In this case they felt that Riedel's struma was not preceded by changes suggestive of struma lymphomatosa. Roulet[21] has recently reported a case in which the findings were typical of Riedel's struma. This patient was operated upon twice with an interval of two and one-half years and the histologic changes in the gland were the same at each examination. Heyd,[22] however, had a patient in whom, in his opinion, struma lymphomatosa preceded typical Riedel's struma, but examination of his evidence makes us feel that, pathologically at least, the lesion was characteristic of Riedel's struma on both occasions. As far as we know, there has not been a case of struma lymphomatosa reported in which the histologic changes have been described twice, the second time several months or years after the first examination. Clute, Eckerson, and Warren[14] had one patient who was operated upon twice, the second time after an interval of two years, but in their paper they make no mention of the histologic findings on each occasion. Since the case is classed as struma lymphomatosa it may be inferred that the pathologic changes were the same at each examination.

In Case 10 the clinical symptoms and signs as well as the histologic changes at the second admission were practically identical with those found at the

time of the original examination. These findings thus shed new light on the controversial question of the possible relationship of Riedel's struma and struma lymphomatosa. They distinctly favor the contention that the two types of change are separate, distinct, and in no way related. The presence of slightly more sclerosis of the gland at the time of the second examination may be in some measure the result of the previous operation. The fundamental clinical symptoms of weakness, easy fatigability, tightness in the neck, dyspnea, and dysphagia, and the histologic changes, consisting of lymphoid infiltration with lymph nodule formation and the characteristic appearance of the acini, were still the same at the second examination as they were at the first. If struma lymphomatosa were the precursor of Riedel's struma, sufficient time had certainly elapsed in this case for the changes to have become evident, because clinically Riedel's struma has been shown to be generally of shorter duration than struma lymphomatosa, and its course is much more rapid.

Clinically and pathologically, therefore, we believe Riedel's struma and struma lymphomatosa (Hashimoto) to be separate diseases of different etiology and producing different clinical symptoms. There is no valid reason for considering the latter to be an earlier stage of the former. The two lesions, while not uncommon, occur with sufficient rarity to warrant very careful clinical and pathologic study of every possible case. We hope that further investigations will establish definitely the etiology of the lesions and thus settle once and for all the moot question of a possible relationship of the diseases to each other.

SUMMARY

(1) Twelve cases of benign struma are presented, four of the type described by Riedel and four of the type described by Hashimoto, with four associated with foreign body giant cells. Attention is directed to the possibility that future study may show that cases which are classified as Riedel's struma are in reality a group of different types of chronic thyroiditis.

(2) There is a growing tendency to regard Riedel's struma and struma lymphomatosa as separate and distinct entities. With this concept we are in agreement.

(3) Clinical differences between the two types are presented together with the pathologic changes seen in each type.

(4) Corresponding histologic findings in a case of struma lymphomatosa studied twice, the second time after an interval of two years, strongly supports the thesis that this type of change is distinct and separate from the type described by Riedel.

The authors are indebted to Dr. George E. Beilby, Albany, N. Y., for his helpful advice and for permission to present these cases from his private practice. To Dr. Allen Graham, Cleveland, Ohio, they also express their appreciation for his review of the material used in this study and for his suggestions.

REFERENCES

[1] Hashimoto, H.: Zur Kenntnis der Lymphomatosen Veranderungen der Schilddruse (Struma lymphomatosa). Arch. f. klin. Chir., **97,** 219–248, 1912.

[2] Riedel, B. M. C. L.: Die chronische zur Bildung eisenharter Tumoren fuhrende Entzundung der Schilddruse, Verhandl. d. deutsch. Gesellsch. f. Chir., **25,** 101, 1896.

[3] Ewing, James: Neoplastic Diseases, Ed. **2,** 908, Philadelphia, W. B. Saunders Co., 1922.

[4] Graham, A.: Riedel's Struma in Contrast to Struma Lymphomatosa (Hashimoto). West. Jour. Surg., **39,** 681–689, September, 1931.

[5] Lee, J. G.: Chronic Nonspecific Thyroiditis, Arch. Surg., **31,** 982–1013, December, 1935.

[6] Boyden, A. M., Coller, F. A., and Bugher, J. C.: Riedel's Struma. West. Jour. Surg., **43,** 547–563, October, 1935; also in Trans. Amer. Assoc. for Study of Goiter, 35–62, 1935.

[7] Graham, A.: Personal communication.

[8] Tearnan, C. H.: Riedel's Struma. Illinois Med. Jour., **66,** 475–478, November, 1934.

[9] King, B. T.: Thyroiditis. West. Jour. Surg., **41,** 391–398, July, 1933.

[10] Clute, H. M., and Lahey, F. H.: Thyroiditis. ANNALS OF SURGERY, **95,** 493–498, April, 1932.

[11] Smith, L. W., and Clute, H. M.: Chronic Ligneous Thyroiditis (Riedel's Struma), Amer. Jour. Med. Sci., **172,** 403–416, September, 1926.

[12] Bohan, P. T.: Ligneous Thyroiditis Associated with High Grade Dental Infection. Med. Clin. N. Amer., **7,** 1069–1074, January, 1924.

[13] Searls, H. H., and Bartlett, E. I.: Thyroiditis. Calif. and West. Med., **24,** 639–642, May, 1926.

[14] Clute, H. M., Eckerson, E. B., and Warren, S.: Clinical Aspects of Struma Lymphomatosa (Hashimoto). Arch. Surg., **31,** 419–428, September, 1935.

[15] Clute, H. M., and Warren, S.: The Prognosis of Thyroid Cancer. Surg., Gynec., and Obst., **60,** 861–874, April, 1935.

[16] Williamson, G. S., and Pearse, I. H.: The Pathological Classification of Goiter. Jour. Path. and Bacteriol., **28,** 361–367, April, 1925.

Ibid.: Lymphadenoid Goiter and Its Clinical Significance. Brit. Med. Jour., **1,** 4–5, January 5, 1929.

[17] McCarrison, R.: Note on Experimental Production of Lymphadenoid Goiter in Rats. Brit. Med. Jour., **1,** 5–6, January 5, 1929.

[18] Shaw, A. F. B., and Smith, R. P.: Riedel's Chronic Thyroiditis; with a Report of Six Cases and a Contribution to the Pathology. Brit. Jour. Surg., **13,** 93–108, July, 1925.

[19] Poer, D. H., Davison, T. C., and Bishop, E. L.: Struma Lymphomatosa (Hashimoto); Report of a Case. Amer. Jour. Surg., **32,** 172–175, April, 1936.

[20] Perman, E., and Wahlgren, F.: Case of Chronic Thyroiditis (Riedel). Acta Chir. Scandinav., **61,** 535–542, 1927.

[21] Roulet, Frederic: Über eigenartige Gefässbefunde bei chronisher Thyreoiditis (eisenharte Struma Riedel). Virchows Arch. f. path. anat., **280,** 640–648, April, 1931.

[22] Heyd, C. G.: Riedel's Struma; Benign Granuloma of the Thyroid. Surg. Clin. N. Amer., **9,** 493–513, June, 1929.

[23] Vogel, W.: Über Strumitis, Struma spezifica und Riedelsche Struma. Ergebn. d. Chir. u. Orthop., **23,** 317–350, 1930.

[24] Bothe, F. A.: Early Stage of Riedel's Struma. Surg. Clin. N. Amer., **11,** 1445–1448, December, 1931.

[25] Crane, W.: Chronic Thyroiditis. Calif. and West. Med., **35,** 443–446, December, 1931.

[26] Bruce, H. A.: Case of Thyroiditis Simplex (Riedel's Tumor). ANNALS OF SURGERY, **94,** 562, October, 1931.

[27] Kreuzbauer, F. H.: Die Thyreoiditis chronica. Ein weiterer Beitrag zur Kenntnis der Riedelschen "eisenharte Struma." Arch. f. klin. Chir., **166,** 178–182, August, 1931.

[28] Kreuzbauer, F. H.: Die Thyreoiditis chronica. Ein Beitrag zur Kenntnis der Riedelschen "eisenharten Struma." Arch. f. klin. Chir., **163,** 86–107, 1930.

[29] Prati, Mario: Sul morbo di Riedel. Arch. ital. di chir., **29,** 93–111, May, 1931.

[30] Traum, E.: Zur Frage des Rezidivs bei der sogenannten Riedelschen eisenharten Struma. Deutsch. Ztschr. f. Chir., **231,** 635–637, July, 1931.

[31] Diez, J.: Tiroiditis lêñosa del Riedel. Prensa Méd. Argent., **18,** 1144–1156, January 30, 1932.

[32] Nestmann, F.: Zur Frage der chronischen Thyreoiditis. Beitr. z. klin. Chir., **156,** 253–262, August, 1932.

[33] Oehler, J.: Zur "eisenharten Struma." Zentralbl. f. Chir., **59,** 1295–1297, May 27, 1932.

[34] White, C. S.: Riedel's Thyroiditis; Report of a Case. Med. Ann. District of Columbia, **1,** 153–155, June, 1932.

[35] Angerer, H.: Über die eisenharte Struma. Zentralbl. f. Chir., **60,** 1885–1889, August 12, 1933.

[36] Melina, F.: Contributo allo studio della tiroidite lignea (Morbo di Riedel). Gazz. Internaz. Med. Chir., **41,** 443–451, August 15, 1933.

[37] Nordland, M., and Larson, L. M.: Goiter Clinic; Presentation of Ten Unusual Cases of Thyroid Disorders. Minnesota Med., **16,** 536–539, August, 1933.

[38] Eisen, D.: Riedel's Struma with a Report of Seven Cases. Canadian Med. Assn. Jour., **31,** 144–147, August, 1934.

Ibid.: Relationship between Riedel's Struma and Struma Lymphomatosa (Hashimoto). Canadian Med. Assn. Jour., **31,** 147–150, August, 1934.

[39] Howard, L. L.: Struma Lymphomatosa (Hashimoto). Amer. Jour. Surg., **23,** 565–569, March, 1934.

[40] Lester, C. W.: Three Tumors of the Thyroid. Amer. Jour. Cancer, **21,** 103–109, May, 1934.

[41] Polowe, D.: Struma Lymphomatosa (Hashimoto). Associated with Hyperthyroidism; Report of a Case with Clinical and Histipathologic Study. Arch. Surg., **29,** 768–777, November, 1934.

[42] Seed, L.: Discussion of the paper by Tearnan.[8]

[43] Benson, B. B.: Riedel's Struma. Amer. Jour. Surg., **27,** 361–367, February, 1935.

[44] Emerson, C.: Struma Lymphomatosa (Hashimoto); with Report of Ninth Case. Nebraska Med. Jour., **20,** 58–60, February, 1935.

[45] Gilchrist, R. K.: Chronic Thyroiditis. Arch. Surg., **31,** 429–436, September, 1935.

[46] Mallory, T. B.: Case Records of the Massachusetts General Hospital; Presentation of a Case. New England Jour. Med., **213,** 1140–1143, December, 1935.

DUODENAL DIAPHRAGM

EARL G. KRIEG, M.D.
DETROIT, MICH.

A DISCUSSION of all discoverable cases of intrinsic malformations of the duodenum due to diaphragmatic lesions is herewith presented. Twenty cases have been reported in the literature, to which list is added another instance of its occurrence.

A clinical differentiation between duodenal diaphragms and areas of stenosis or atresia cannot be made in the first weeks of life, because the clinical pictures may be identical. Later a more definite diagnosis can be made. At all ages, roentgenologic studies aid the clinical findings. In the correction of these lesions certain technical considerations improve the result obtained.

Robert Boyd,[1] in 1845, reported the first case of obstruction of the duodenum due to a double diaphragm. Since then additional instances of diaphragm have been reported alone or contained in a series of other intestinal malformations.

Although various operative procedures had been undertaken for congenital duodenal obstructions, it was not until 1911 that a jejunoduodenostomy for an atresia of the duodenum was successfully performed by P. Fochens[13] in a seven day old child. Ladd,[21] in 1933, and Morton,[25] in 1935, reported the first and second cases of membranous diaphragms operated upon successfully.

The experience of Fochens, Edington,[11] Ernst,[12] Ladd and others has shown that a successful outcome depends upon short-circuiting of the bowel stream by the most direct method at the primary operation and by the use of nonabsorbable sutures. In 1935, Morton reported a case which demonstrated the practicability of removing the lesion without employing a short-circuiting procedure.

Etiology.—E. Kreuter,[20] J. Tandler,[35] H. Forssner,[14] and Marshall and Balfour[22] have observed in the five weeks embryo that the primitive gut closes solidly with a proliferation of epithelial cells which shortly begins to recede by a process of vacuolization until the bowel takes on its final histologic structure. They believe that the intrinsic malformations are due to the faulty recession of these cells. H. Schriddle,[29] Theremin,[37] Dohrn[10] and others do not believe this to be true and attribute the malformations to fetal peritonitis. In view of the fact that diaphragmatic obstructions are composed of normal bowel sructures it would appear more logical to accept the former explanation in the cases under discussion.

Classification.—Our review of the literature emphasizes the necessity for a standard classification of these lesions. H. Forssner presents a classification

Submitted for publication September 8, 1936.

which is complete and scientific (Fig. 1 and Table I). We suggest that it be used in all cases to aid investigation.

TABLE I

FORSSNER'S CLASSIFICATION OF DUODENAL MALFORMATIONS

Diaphragm:	Complete
	Incomplete
Stenosis:	Complete
	Incomplete
Atresia:	Blind ends connected by a band.
	Blind ends unconnected.

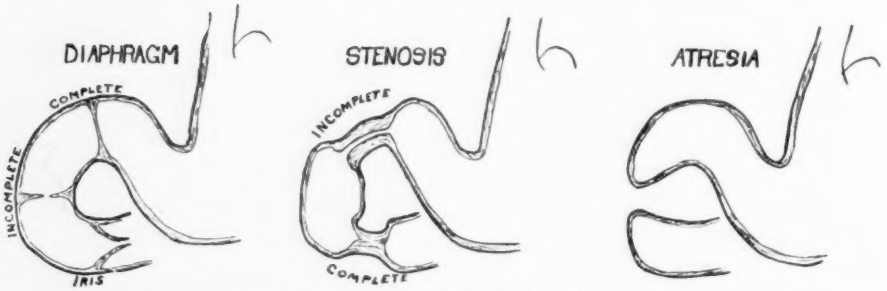


FIG. 1.—Drawings illustrating Forssner's classification of intrinsic duodenal malformations.

Statistical Analysis.—All intrinsic malformations of the intestinal tract, exclusive of anal atresias, are very uncommon. The combined series of consecutive cases of newborn infants investigated by E. Theremin, De Sanctis and Craig,[9] Thorndike[38] and Von Koss[39] total 688,992 and in this group only 31 cases of intrinsic duodenal malformations were found, an incidence of 1 in 21,580. This proportion does not give an accurate picture for we find that more than one-half of the cases of diaphragm come under observation later in life.

The relative frequency of duodenal diaphragms to other duodenal malformations is shown in Table II.

TABLE II

PROPORTION OF DUODENAL DIAPHRAGMATIC OBSTRUCTIONS

Author	Duodenal Series	Cases of Diaphragm	Percentage
Spriggs	92 cases	2	2.0%
Garvin	113 cases	1	0.8%
Ladd	40 cases	1	2.5%

The sex incidence is about equal in this series; there are seven males, eight females and six cases in which no sex is mentioned.

Diaphragmatic obstructions may be encountered throughout life. The youngest reported is stillborn and the oldest 70. Symptoms begin in approximately 38 per cent of the cases during the first two weeks of life, 10 per cent occur between three and eight months; 24 per cent occur between one and

eight years; 29 per cent occur after 24 years. In contrast, the cases of stenosis rarely live beyond four weeks, the majority succumbing during the first two weeks. G. Lennox and C. Cautley report the only two cases of stenosis living beyond one year encountered in the literature.

Pathology.—The external appearance of the bowel wall in the region of the diaphragm is normal to inspection and palpation with the exception of some degree of dilatation and hypertrophy which depends upon the degree and duration of the obstructive lesion. Realization of this absence of external serosal pathology is important because we find that in many of the reported cases the lesion was not suspected during operation.

In this series the location of the diaphragm in relation to the ampulla of Vater is comparable to that of other intrinsic malformations. The lesion is proximal to the ampulla in 45 per cent, opposite to it in 20 per cent, distal to it in 25 per cent and at the duodenojejunal junction in ten per cent.

The gross structure of a diaphragm is that of a thin partition extending transversely across the bowel lumen, and it may be complete or contain an aperture which varies in size. A variation occasionally seen is the so-called iris type of lesion which projects down the canal like the finger of a glove. The base of the septum is usually from 1 to 3 Mm. in thickness and becomes thin in the central zone.

Microscopically, the bowel wall on either side of the lesion is normal. The diaphragm is composed of a continuation of the mucous membrane and the submucosa. A few muscle fibers have been found in the base of the diaphragm and in Seidlin's[31] case, islands of pancreatic tissue.

The Size of the Aperture.—The relationship of the size of the aperture to the age period of the onset of serious symptoms is definite and constant in the 18 cases that have been completely described (Table III). The explanation of this relationship can only be theoretical, and apparently involves at least three factors: First, the size of the aperature in the diaphragm does not increase in proportion to the normal lumen of the bowel and symptoms appear when the disproportion becomes favorable for obstruction. Second, G. Buchanan[3] has pointed out the relationship of solid foods added to the infant's diet. Seidlin's patient, two and one-half years of age, died of acute obstruction caused by a tangled mass of greens and hominy. Third, faulty mechanical functioning of the bowel wall results from an incomplete development of muscular and nervous elements.

Symptomatology.—The symptoms of this condition are clinically those of pyloric obstruction and may be acute or chronic. They usually begin at an early age and their duration ranges from a few hours in the youngest (34 per cent), to many years in the older cases. The symptoms may be constant or there may be intervals of days or months between attacks.

Vomiting is the most frequent and usually the first symptom; it may be regular or projectile and occur after every meal or at the end of the day. Nausea accompanies vomiting in most cases old enough to complain.

Pain in the upper right quadrant or umbilical region is present in most

TABLE III

EIGHTEEN CASES SHOWING DIRECT RELATION OF SIZE OF APERTURE TO THE ONSET OF SERIOUS SYMPTOMS

Age of Onset	Size of Aperture					
	Complete	1–2Mm.	2–3Mm.	4–7Mm.	8Mm.	10–15Mm.
5 days or less	7					
14 days		3				
1 mo.–1 yr			2			
1–10 yrs.				2		
20 yrs. and over					2	
Accidental autopsy findings						2

cases and may occur at the time of vomiting. The prone position may give relief.

Constipation may be present varying in degree from mild to severe, and may be constant or intermittent.

Visible peristalsis is present in 25 per cent of the cases.

Distention, weakness, dizziness, fever, belching, tumor mass, and sudden death are the more infrequent signs mentioned in the literature.

Differential Diagnosis.—The differential diagnosis corresponds to that of the most usual symptom, *i.e.*, vomiting, which is comprehensively discussed by H. C. Cameron.[4] I desire to stress only the unusual conditons most likely to be confused with diaphragm.

(1) Peritoneal bands are most frequently found in the duodenojejunal region. One-third of Ladd's series, composed of intrinsic and extrinsic lesions, were due to bands.

(2) Atresias constitute about 85 per cent of the intrinsic lesions and cause serious symptoms in the first five days after which period they may be ruled out.

(3) Stenotic cases comprise about 13 per cent of the intrinsic lesions. When the stenosis is complete, the appearance of symptoms is the same as in the atresias. When the stenosis is incomplete, the size of the aperture determines the age incidence of the onset of serious symptoms. I have found no case older than three years and relatively few are older than three months; the majority are discovered in the first month.

(4) Hyperplastic pyloric stenosis is most frequently found in the male infant but cases are being reported showing that this condition is also found in the adult.

Diagnosis.—The history is the most important aid to diagnosis. The age of the individual is also important.

Physical examination may reveal upper abdominal distention and visible gastric peristalsis.

Roentgenologic examinations may show complete occlusion or dilatation

of the stomach and duodenum and a "to and fro" peristalsis proximal to the lesion.

Treatment.—The treatment of diaphragmatic obstructions of the duodenum is surgical. Duodenojejunostomy is preferable to gastrojejunostomy. The experiences of Ladd and others bear out the soundness of these fundamentals. Simple enterostomy has always been attended by disaster.

Morton, in a recently reported case, has recorded the removal of the diaphragm by electrodesiccation after direct exposure; the result was excellent. I believe this method is preferable to all others where it can be employed.

Silk is the suture material that has been used exclusively by the pioneer

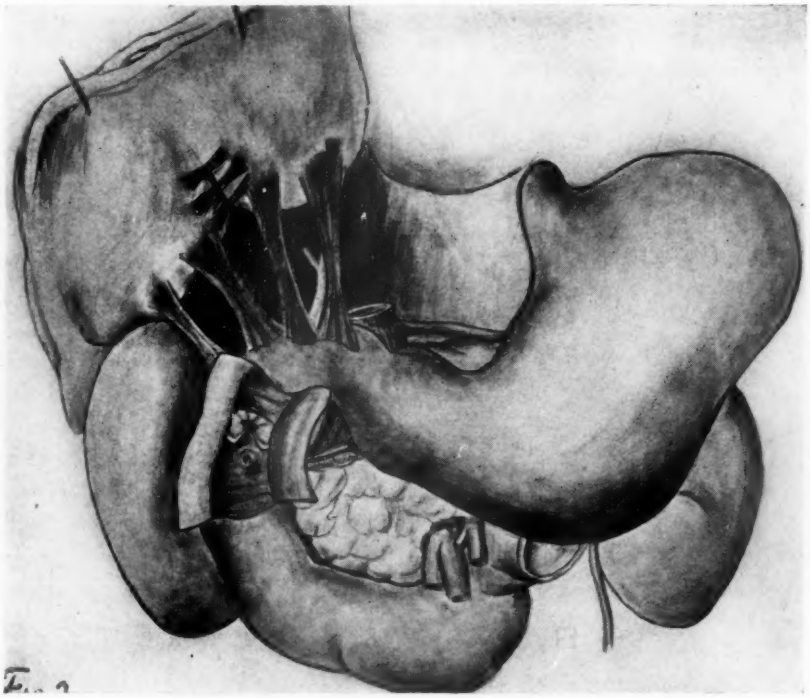


FIG. 2.—Drawing indicating the pathology presented.

surgeons in this field, and by all others who have had any large experience with similar cases.

The fact that nonabsorbable sutures contribute to a successful outcome in cases of chronic obstruction has been firmly impressed upon me by Terry and Kilgore's[36] case and one other in my own experience, which was operated upon for a duodenal stricture due to ulcer. In both instances autopsy revealed that the anastomosis had broken down because the catgut sutures were absorbed before adequate healing had taken place. Ladd uses only one row of silk sutures in the anastomisis to expedite the operation in infants.

Pre- and postoperative treatment is the same as that given any other case of intestinal obstruction and is of the utmost importance.

Case Report.—Mrs. L. G., white, age 36, was first seen in November, 1931. Fifteen years previously vague upper abdominal pains occurred with some regularity. At this time the pylorus was explored and the appendix removed. Although these attacks did not disappear, they required little treatment until after a cholecystectomy for stones in 1927, when the vague pains became severe and crampy and were accompanied by vomiting, diarrhea and frequency of urination. These attacks occurred at approximately monthly intervals and lasted ten to 14 days. In collaboration with Dr. H. Kullman, repeated investigations and painstaking observations revealed only the objective signs of postoperative adhesions causing distortion of the duodenal cap but no obstruction.

General physical examination was essentially negative except for a regularly occurring temperature of 99.2° F.; bilateral reddened tonsil tags, two devitalized molars, two abdominal scars of previous operations and some tenderness over the left renal area.

Repeated renal studies, including pyelograms and cultures, blood studies, gastric analyses, proctoscopic and stool examinations and barium enemas were entirely negative.

At exploratory operation, November 10, 1932, adhesions were found and liberated. Other dense adhesions involved the liver, duodenum, omentum and the anterior abdominal wall. A healed scar was found in the duodenal wall and an exploratory incision was made in this area. At about 10 cm. below the pyloric vein the finger encountered a perforated membranous diaphragm having an aperture about 8 Mm. in size (Fig. 2). There was no outward evidence of its location. There was no evidence of ulcer. The exploratory wound in the bowel was closed and a short loop antiperistalic gastrojejunostomy was performed using three rows of 00 chromic catgut.

Her convalescence was uneventful and she was discharged on the fourteenth day. Since operation gastric symptoms of pain and vomiting have ceased. Six months later a roentgenogram revealed the stoma to be functioning well.

COMMENT.—The first ten cases were diagnosed at autopsy and no operation was considered. Of this group Silcock's[33] and Moore's[23] cases gave no symptoms referable to the duodenal pathology which was accidentally discovered during routine autopsy for another condition. Terry and Kilgore's[36] case was operated upon for duodenal obstruction but did not survive when the anastomosis effected by the use of catgut broke down five days later; the final diagnosis was made at autopsy. The next six cases that were operated upon were explored and the abdomen closed without discovering the condition; in two of these cases a subsequent jejunostomy was performed and even then the lesion was not suspected! Morton's[24] first case was complicated by an incarcerated hernia near the ligament of Trietz which was thought to have caused obstruction. It is these cases that serve to emphasize several of the points discussed above. The last three cases recovered following operation.

SUMMARY.—(1) Twenty-one cases of membranous diaphragmatic obstruction of duodenum are presented and discussed.

(2) A uniform method of classification is urged.

(3) Over 50 per cent of these cases develop serious symptoms after the first year of life. The size of the aperture apparently determines the time of onset.

(4) All cases over ten years of age having an intrinsic congenital obstruction of duodenum have been diaphragmatic lesions.

(5) The lesion cannot be detected without opening the lumen of the gut. The only clue to its presence is a dilated proximal segment.

TABLE IV

ANALYSIS OF CASES FOUND IN THE LITERATURE

Author	Date Reported	Sex	Age	Location (Re. Ampulla)	Size of Aperture	Operative Procedure	Confirmation at Operation	Confirmation at Autopsy
(1) Boyd, R.[1]	1845	F	Stillborn	Double diaphragm	None–	None	—	Yes
(2) Buchanan, G.	1861	?	18 mos.	Proximal	2.5 Mm.	None	—	Yes
(3) Moore, N.[23]	1884	M	40 yrs.	Duod. jej. junct.	10–15 Mm.	—	—	Accidental
(4) Silcock[33]	1885	F	34 yrs.	Proximal	15 Mm.	None	—	Accidental
(5) Galton, J.[15]	1893	?	1½ days	Distal	None	None	—	Yes
(6) Champneys and Power[6]	1897	?	5 days	Proximal	None	None	—	Yes
(7) Wyss, M. O.[41]	1900	M	1½ days	Opposite	None	None	—	Yes
(8) Shaw and Baldorf[32]	1907	F	13 days	Distal	Small	None	—	Yes
(9) Spriggs[34]	1912	?	9 mos.	Proximal	?	None	—	Yes
(10) Spriggs	1912	M	14 days	Duod. jej. junct.	1–3 Mm.	None	—	Yes
(11) Terry and Kilgore	1916	M	24 yrs.	Proximal	?	Post. gastro-enter.	—	Yes
(12) Schroder, C.[30]	1921	M	14 wks.	Proximal	3 Mm.	(1) Exploratory (2) Jejunostomy	— —	Yes
(13) Morton, J. J.[24]	1923	M	1 day	Proximal	None	Release, paraduodenal hernia	—	Yes
(14) Nagel, G.[27]	1925	M	70 yrs.	Proximal	8 Mm.	Exploratory		Yes
(15) Seidlin, S.	1925	F	2½ yrs.	Opposite	7 Mm.	None	—	Yes
(16) Thorndike, A.	1927	?	17 days	Opposite	1 Mm.	(1) Exploratory (2) Jejunostomy	—	Yes
(17) Garvin, J.[42]	1928	?	5 days	Distal	None	None	—	Yes
(18) Cannon and Halpert[5]	1929	F	8 yrs.	Opposite	4 Mm.	Exploratory		Yes
(19) Ladd, W.	1933	F	8 yrs.	3rd duod.	?	Duod-jejunostomy	Yes	—
(20) Morton, J. J.	1935	F	5 days	2nd duod.	None	Electrodesiccation	Yes	—
(21) Krieg, E.[19]	1936	F	32 yrs	Proximal	8 Mm.	Post. gastro-enter.	Yes	—

(6) Direct removal, duodenojejunostomy or gastro-enterostomy are the procedures of choice in order of their desirability.

(7) Nonabsorbable sutures are advisable.

BIBLIOGRAPHY

[1] Boyd, Robt.: Description of a Malformation of the Duodenum. Lancet, **1**, 648, 1845.

[2] Braun: Ueber de Angeborenen Verschlus des Dunndarms in Seine Operative Behandlung. Beitr. Z. klin. chir., **34**, 993, 1902.

[3] Buchanan, G.: Malformations of Duodenum in Children. Tr. Path. Soc. London, **12**, 121–129, 1816.

[4] Cameron, H. C.: Differential Diagnosis of Vomiting. Brit. Med. Jour., **1**, 765, 1925.

[5] Cannon, P. R., and Halpert, B.: Congenital Stenosis of Third Portion of Duodenum with Acute Occlusion and Rupture of Stomach. Arch. Path., **8**, 611, July–December, 1929.

[6] Champneys, F. H., and Power, D'Arcy: Occlusion of Duodenum by Complete Transverse Septum. Brit. Med. Jour., **1**, 718, 1897.

[7] Cordes, L.: Arch. Ped., **18**, 410, 1901.

[8] Davis, D. L., and Poynter, C. W.: Congenital Occlusions of Intestine. Surg., Gynec., and Obstet., **34**, 35, 1922.

[9] De Sanctis and Craig: Congenital Duodenal Stenosis and Atresia. Am. Jour. Dis. Child., 811, April, 1929.

[10] Dohrn: Jahrb. f. Kinderheilt. (N.S 6), 216, 1868.

[11] Edington: Congenital Occlusions of Oesophagus and Lesser Bowel. Glasgow Med. Jour., **80**, 16, 1913.

[12] Ernst, N. P.: A Case of Congenital Atresia of Duodenum Treated Successfully by Operation. Brit. M. Jour., **1**, 644, 1916.

[13] Fochens, P.: Ein Operativ Geheilter Fall Von Congenitaler Dunndarmsatresie. Zentral. f. Chir., 532, 1911.

[14] Forssner, H.: Die Angeborenen Darm und Oesaphagusatresien.. Merkel u Bonnets, Anatomishe Hefte (No. 102), **34**, 1060, 1907.

[15] Galton, J.: Congenital Occlusion of Duodenum. Guy's Hosp. Rep., **50**, 221, 1893.

[16] Gordon, L.: A Case of Congenital Stenosis of Duodenum. Brit. Jour. Surg., **18**, 331–332, 1930–1931.

[17] Judd, E. S., and Puestow, C. B.: Chronic Duodenal Obstruction. Surg. Clin. N. Amer., **13**, No. 4, 897, August, 1933.

[18] Keith, A.: Constriction and Occlusion of Alimentary Tract of Congenital or Obscure Origin. Brit. Med. Jour., 301, January 29, 1910.

[19] Krieg, E. G.: Hypertrophic Stenosis of Pylorus in an Adult. Jour. Mich. State Med. Soc., March, 1936.

[20] Kreuter, E.: Zur Aetiologie Der Congenitalen Atresien Des Darms u Oesophagus. Arch. f. klin. Chir., **88**, 303, 1909.

[21] Ladd, Wm. E.: Congenital Obstruction of Small Intestine. J.A.M.A., **101**, No. 19, p. 1453, 1933.

[22] Marshall and Balfour: Quoted by Edington.

[23] Moore, N.: Multiple Diverticula of Small Intestine with Congenital Stricture of Duodenum. Tr. Path. Soc. London, **35**, 202, 1884.

[24] Morton, J. J.: Atresia of the Duodenum. Am. Jour. Dis. Child., **25**, 371–378, May, 1923.

[25] Morton, J. J.: Surgical Care of Patients in the Extremes of Life. Am. Jour. Surg., **30**, 92–108, October, 1935.

[26] Norton, J. J.: Personal communication.

[27] Nagel, Gunther: Unusual Conditions in the Duodenum. Arch. Surg., **2**, 529, 1925.

[28] Robertson, G.: Acute Dilatation of Stomach and Intestinal Tube with Consideration of "Chronic Doudenal Ileus." Surg., Gynec., and Obstet., **40,** 206, February, 1925.
[29] Schriddle, H.: Ueber de Epithelproliferationen in der embryonem Menschlichen Speiserohre. Virchows Arch., **191,** 179, 1908.
[30] Schroder, C. H.: Congenital Obstruction of Duodenum. J.A.M.A., **78,** 1037, 1921.
[31] Seidlin, S. M.: Congenital Stenosis of Duodenum. Arch. Ped., **24,** 813, 1907.
[32] Shaw, H. L., and Baldorf, L. K.: Congenital Stenosis of Duodenum. Arch. Ped., **24,** 813, 1907.
[33] Silcock, A. Q.: Epitheliona of Ascending Colon; Entercolitis; Congenital Duodenal Septum with Internal Diverticulum. Tr. Path. Soc. London, **36,** 207, 1885.
[34] Spriggs, N. J.: Congenital Intestinal Occlusion. Guy's Hosp. Report. **66,** series iii, p. 143, 1912.
[35] Tandler, Jul.: Ueber die Entwichlung des Menschlicken Duodenums in Fruhen Embrionalstadien. Morphol. Jahrbuch., **24,** 187–216, 1900.
[36] Terry, W. I., and Kilgore, A. R.: Congenital Stenosis of Duodenum in an Adult. J.A.M.A., **66,** 1774, 1916.
[37] Theremin, E.: Ueber Congenital Occlusion des Dunndarms. Deutsch. Ztschr. f. Chir., **7,** 34, 1877.
[38] Thorndike, A.: Duodenal Atresias and Stenosis in Infancy. Boston Med. and Surg. Jour., **196,** 763, 1927.
[39] Van Koos, A.: Congenital Atresias of Duodenum. Jahrb. f. Kinderh., **93,** 240, 1920.
[40] Weber, W.: Zu Kauistik der Angeborenen Atresie des Duodenums. Med. Klin., **6,** 1294, 1910.
[41] Wyss, M. O.: Ueber Congenitale Duodenalatresen. Bruns Beitrage z. klin. Chir., **26,** 631, 1900.
[42] Garvin, J. A.: Congenital Occlusion of Duodenum by Complete Diaphragm. Am. Jour. Dis. Child., **35,** 109, 1928.

THE TREATMENT OF ACUTE APPENDICITIS*

GEORGE H. BUNCH, M.D., AND ROGER DOUGHTY, M.D.
COLUMBIA, S. C.

THE frequency and seriousness of acute appendicitis have prompted us to prepare a résumé of our own experiences, and those of others, with the principles which should govern its treatment and the results obtained. Chronic appendicitis has not been included, although we make a practice of removing the appendix in every laparotomy if the condition of the patient warrants, and we feel that this is good surgery, for with but little additional risk, the patient is freed of a structure that is most prone to disease.

In the treatment of acute appendicitis there should be proper application of both the art and the science of surgery if operation is to give the patient the best chance of recovery. In recent literature there is much discussion and controversy over *when to operate*. We wish to emphasize that *how to operate* is even more fundamentally important. We believe that the great difference in the morbidity and mortality rates given in the various series of cases reported depends upon essential differences in the application of basic principles which, if understood, would tend to standardize treatment and to lower mortality.

Classification.—Much of the present confusion about acute appendicitis is due to differences in the classification of its stages and complications. This should be simple and unmistakable. Only in this way can understanding be assured and results intelligently compared. We have classified acute appendicitis as:

(A) Acute appendicitis—not perforated.
(B) Acute appendicitis—gangrenous and perforated.
(1) Recent perforation.
(2) Perforation with diffuse spreading peritonitis.
(3) Perforation with localized abscess.

Each of these four conditions presents problems, both in operative and nonoperative management, peculiarly its own. The patient's best chance of recovery depends upon proper understanding by the surgeon of the pathology present and the use by him of the treatment best suited to the individual case.

Acute Appendicitis—*Not Perforated:* We agree with others that acute appendicitis is a surgical emergency demanding early operation before perforation occurs. However, we do not think immediate operation is imperative as it is in acute hemorrhage, strangulated hernia or acute perforation of peptic ulcer. Thus, we feel that, if the patient is admitted after midnight, morphine should be given to rest the intestine and operation deferred until early morn-

* Read before the Southern Surgical Association, Edgewater Park, Miss., December 15, 1936.

ing. A sleepy operating crew does not function well, and an aseptic technic is jeopardized. We employ the McBurney muscle-split incision and invaginate the appendix stump. Contrary to the belief[1, 7, 8] that the inflammatory exudate, so often found within the peritoneal cavity at operation, is protective and germicidal, we feel that it may be harmful and should always be removed. We have lost a patient from pelvic abscess in which this was not done.

The exudate from appendicitis has not the ropy viscid consistency of that found within the peritoneal cavity after an acute perforation of a gastric or a duodenal ulcer. We attribute this characteristic to the reaction of the peritoneum to the acid irritation. When the exudate is of this nature, particularly if it is without colon odor and the symptoms are atypical, an ulcer should be sought for and the perforation closed; otherwise the death will be attributed to appendicitis.

If the appendix is gangrenous, after the peritoneum and muscle have been closed with catgut, the skin and fascia of the external oblique should be loosely approximated with interrupted silkworm sutures. A wick of rubber dam placed under the fascia to the muscle and brought out through a stab wound insures drainage of the wound in the abdominal wall and prevents suppuration and sloughing of the fascia, a not infrequent complication if this is not done. Wound contamination from a gangrenous appendix is much more apt to cause suppuration and slough than that from salpingitis or tubo-ovarian abscess. Even when grossly infected a McBurney incision closed in this way heals without hernia.

Early Perforation.—There are no criteria by which we may be sure when perforation occurs in an acutely congested appendix. However, relief from pain, as intra-appendiceal pressure is eased by perforation, is quite suggestive. In our experience, perforation occurs within 72 hours of the onset of symptoms. If perforation has not taken place within that time, symptoms improve as the inflammation subsides and resolution begins. The tendency to perforation is lessened by narcosis and is definitely increased by catharsis.

After perforation there is gross soiling of the adjacent peritoneum by appendiccal contents. The great resistance of the peritoneum to infection is shown by its ability to overcome this contamination in most cases if appendicectomy is performed early and continued soiling prevented. This is significant, for it explains the good results obtained without drainage in this class of cases.[3] However, we believe it is safer to drain all perforated cases. A rubber protected cigarette drain, with the gauze cut flush, brought through a stab wound does no harm and prevents pocketing and abscess formation. It should not come in contact with small intestine and, if possible, should hug the parietal peritoneum throughout its course.

Table I shows the mortality in acute appendicitis, unruptured and with early perforation, which has occurred in the work of one of us (G. H. B.). It also shows the total number of cases operated upon. It is to be noted that the later years have a lower mortality, due to increased experience of the surgeon and to the better condition of the patients when first seen.

TABLE I

MORTALITY RATE IN ACUTE APPENDICITIS—ALL STAGES

Period	Number of Cases	Deaths	Mortality
1911–1929 inclusive—19 years	1,119	35	2.8%
1930–1935 inclusive— 6 years	936	17	1.8%
1919–1935 inclusive—17 years	2,055	50	2.4%
Acute, not perforated	1,593	4	0.25%
Early perforation	181	5	2.8%

Perforation with Diffuse Peritonitis.—After perforation, when appendicectomy is not performed, if nature succeeds in limiting the infection by a plastic exudate, a localized abscess forms. Unfortunately, however, when the power of localization is impaired, as in pregnancy, and infancy, when the infecting organisms are too virulent, and when contamination is too great, as after catharsis or when the patient's resistance is low, the conservative power of nature is overcome and diffuse peritonitis begins. The incubation time that must elapse from perforation and contamination to the beginning of peritonitis is of fundamental importance in the treatment of the patient. After this time has passed, every vital force of the patient is needed to combat the infection. The contamination phase is not ended until a pyogenic membrane has formed.

Stanton[5] has graphically shown that, in a compilation of cases from recent literature, after the attack has begun, the mortality rate of acute appendicitis varies greatly with the time that elapses before operation. The mortality per cent is greatest when operation is performed on the third, fourth, fifth and sixth days after onset (Table II). From these figures if the rule—operate before the third day or wait until after the sixth day from onset—were blindly followed, the mortality rate of acute appendicitis would be cut in half. Certainly good judgment in the selection of the best treatment, for the individual case, during these four critical days materially lessens mortality.

TABLE II

MORTALITY RATE RELATIVE TO TIME OF OPERATION

Compiled from the Literature by Stanton[5]

Day of Operation after Attack Began	Number of Cases	Deaths	Mortality Per Cent
1st day	1,507	20	1.3%
2nd day	912	33	3.6%
3rd day	663	56	8.9%
4th day	365	46	12.9%
5th day	442	49	11.6%
6th day	346	29	8.4%
7th, 8th or 9th day	178	5	2.8%
10th day or later	288	7	2.4%
Total	4,692	245	5.22%

Postponing operation in cases of diffuse peritonitis until resistance has increased and localization is accomplished is sound judgment. These patients when first seen on the fourth or fifth day after the onset of symptoms, with distended abdomen, furred tongue, rapid pulse, nausea and often semi-delirium, are toxic and dehydrated, they hang, literally, between life and death. Operation upon them, too often, only hastens the end. Our endeavor should be to aid nature in this crisis by not giving anything by mouth, not even water, and by the administration of sufficient morphine to insure physiologic rest of the intestine. In an adult a quarter of a grain of morphine should be given hypodermically every three hours if the respirations are 15 or more per minute. It is difficult to obtain the full therapeutic effect of the drug in a septic patient and maximum doses must be given. This applies even to young children. Gastric lavage or continuous duodenal suction, through an indwelling Levine tube, removes any regurgitated fluid from these viscera, lessens absorption, and insures the escape of gas. Continuous hot stupes applied to the abdomen lessen inflammation and relieve pain. An abundance of normal salt solution with glucose and insulin, given preferably by intravenous drip, prevents dehydration and acidosis. The use of oxygen is helpful and may be life saving in these profoundly toxic patients.

Although under this treatment some patients die of progressive sepsis, there is the consolation that they must also have died from operation and there is the assurance, proved by the experience of an increasing number of surgeons (Guerry,[4] Coller,[2] Stanton[5]), that conservation in this critical period results in a lower net mortality and enables a larger percentage of cases to pass safely through it into the stage of resolution or localized abscess, when operation can be performed with comparative safety.

TABLE III

MORTALITY RATE RELATIVE TO IMMEDIATE VERSUS DELAYED OPERATION

Compiled from the Literature by Stanton[5]

	Number of Cases	Deaths	Mortality
Frank acute appendicitis	1,004	40	3.9%
Clinical peritonitis on admission	113	20	17.69%
Of the 113 cases there were:			
Immediate operation	31	13	42.0%
Delayed operation	82	7	8.5%

There is no doubt that most of the mortality from appendicitis occurs in this group and until the physician and the layman are educated to the fact that cathartics should not be given for abdominal pain, and that patients should reach the surgeon before perforation has occurred, the hope of materially lessening the mortality of appendicitis lies in deferring operation in this group. This is shown by the experience of Guerry[4] (Table IV).

TABLE IV

MORTALITY RATE RELATIVE TO IMMEDIATE VERSUS DELAYED OPERATION

Statistics Compiled by Guerry[4]

	Number of Cases	Deaths	Mortality
Acute appendicitis, ruptured and unruptured	1,770	19	1.07%
Diffuse peritonitis:			
Immediate operation	94	10	10.6%
Deferred operation	139	2	1.43%

Guerry's low mortality in appendicitis is due to the application of this basic principle supplemented by consummate operative skill and to the fact that all the cases in his series have been operated upon by him personally. Although his results have been so excellent that they have not been universally accepted, we who have been present and have assisted with the operations performed by him during 20 of the 30 year period reported upon wish to express our conviction that his figures are sincere. His work in appendicitis began at a time when abdominal surgery was just beginning in the South, and when the diagnosis was too often not made until perforation had already occurred. From this early experience he observed that cases seen after the sixth day from onset were often in a state of early localization and that most of them recovered after operation. Reasoning from this, when cases were first seen with peritonitis after perforation, he waited for localization before operating. We know that his teaching and his practice have appreciably improved the quality of appendicitis work done in Columbia, and are a factor in the mortality rate of 8.3 per cent from appendicitis per 100,000 white population in South Carolina, reported by Dauer and Lilly[6] from the mortality statistics of the United States Bureau of Census as being the lowest in the United States.

TABLE V

APPENDICITIS MORTALITY RATE PER 100,000

New England States	14.9%
North Atlantic States	14.5%
East North Central	16.1%
West North Central	17.4%
South Central States	14.5%
Rocky Mountain States	23.5%
Pacific States	15.4%
South Atlantic States	11.3%
South Carolina	8.3%

Abscess.—An appendiceal abscess is diagnosed by the recognition of a palpable mass in the lower right abdomen following acute appendicitis. It has a definite mortality rate and the operative treatment depends upon the size, location and duration of the abscess. The McBurney incision, modified to meet individual conditions, offers the best approach. It is safer in large

abscesses to be content simply to drain them in the easiest way possible, without entering the free peritoneal cavity. The appendix in these cases may be removed later when infection has disappeared and the patient's general condition is good. In ordinary abscesses the peritoneal cavity should be entered and walled off with moist pads before they are opened. The appendix should be removed if possible. However, in old abscesses when the intestine is fixed by fibrous adhesions, identification of the appendix is difficult and dissection is dangerous. We know a case in which the terminal ilium was unknowingly torn from the cecum and left unrecognized to discharge into the peritoneal cavity, with fatal results. One of us, (G. H. B.) has mistaken the right ureter for the appendix in an old abscess. Fortunately, the severed ends united satisfactorily after suture and the patient recovered. When the appendix is not removed, convalescence is delayed and wound discharge prolonged. Any part of an appendix left may subsequently become acutely inflamed and perforate. If present, fluid in the pelvis should be removed and drainage instituted.

Drains should be protected with rubber dam, and raw gauze should never be left in contact with the small intestine. Even when the abscess is situated among the coils of the small intestine, if gauze is not allowed to touch them, there will be little danger of postoperative obstruction. The drains should be brought out through a stab wound and should not be removed for a week or until the drainage tract has become well established. Although operation upon an appendiceal abscess is in no sense an emergency, it should not be deferred indefinitely. Care must be taken in handling and in transporting the patient who has a large abscess. If it should rupture into the peritoneal cavity, although the patient has acquired some degree of immunity to the infection, the contamination is apt to be so great that the patient may die of septic absorption. Three of the 17 deaths from abscesses reported by one of us (G. H. B.) were from this cause.

TABLE VI

SUMMARY OF THE MORTALITY IN THE VARIOUS GROUPS OF ACUTE APPENDICITIS

	Bunch		Doughty		Total	
	Cases	Mortality	Cases	Mortality	Cases	Mortality
Acute unruptured	1,593	0.25%	204	0	1,794	0.22%
Early perforation	181	2.8%	No data			
Spreading peritonitis	87	27.0%	14	21.4%	101	26.0%
Immediate operation	No data	No data	7	28.6%		
Delayed operation	No data	No data	7	14.3%		
Localized abscess and (or) localized peritonitis	164	8.2%	36	0	230	7.3%
Total ruptured	492	9.9%	50	6.0%	512	9.5%
Total acute, ruptured and unruptured	2,055	2.4%	254	1.18%	2,309	2.29%

Since 1930 one of us (G. H. B.) has used spinal anesthesia almost as a routine in operations performed below the diaphragm. The better relaxation

obtained in spinal anesthesia reduces to a minimum necessary operative manipulation within the abdomen and affords better exposure, cleaner dissection, more accurate control of bleeding and easier wound closure. In perforated cases, infection is not so apt to be spread. Postoperatively there is less nausea, less retention of urine, less distention and less respiratory complications. It is considered a factor in the reduction of the gross mortality in acute appendicitis, from 2.8 per cent, before 1930, to 1.8 per cent since 1930 (Table I).

Cathartics and delay are responsible for most of the mortality in appendicitis. We believe that both the intelligent layman and the physician are becoming appendicitis minded, so that a large proportion of cases are referred for operation early, before perforation has occurred. If the surgeon tactfully but frankly educates the clinician along these lines, his mortality in appendicitis will be reduced by the improved class of risks referred to him. Largely because of this the number of acute appendicitis cases, perforated at the time of admission (G. H. B.), has fallen from 22 per cent, previous to 1930, to 15.5 per cent since 1930, although many of the patients were poor and ignorant, and came from farming and textile industries.

CONCLUSIONS

Acute appendicitis, the most common cause for abdominal operation, still has a death rate which is too high. This, obviously, may be reduced by educating the physician and the layman not to give cathartics when there is abdominal pain and not to delay operation when symptoms begin.

In patients having diffuse peritonitis, when first seen by the surgeon, deferring operation, until immunity is acquired and a localized abscess forms, will materially reduce the mortality of the group in which most of the deaths from appendicitis occur.

Both the peritoneal cavity and the abdominal wall should be drained.

REFERENCES

[1] Murphy, John B.: Surgical Clinics, **2,** No. 1, 60, February, 1913.

[2] Coller, F. A., and Potter, E. B.: The Treatment of Peritonitis Associated with Appendicitis. J.A.M.A., **103,** No. 23, 1753, December 8, 1934.

[3] Shipley, Arthur M., and Bailey, Hugh A.: Treatment of Appendicitis Complicated by Peritonitis. ANNALS OF SURGERY, **96,** No. 4, 537, October, 1932.

[4] Guerry, LeGrand: A Discussion of the Management of Late Suppurative Peritonitis Cases. Paper Read Before Section on Surgery, Southern Medical Association, November 19, 1936. (Not yet published.)

[5] Stanton, E. M.: Acute Appendicitis. Surg., Gynec. and Obstet., **59,** 738, November, 1934.

[6] Dauer, C. C., and Lilly, G. D.: Am. J. Surg., New Series, **30,** No. 1, 119, October, 1935.

[7] Pattison, A. T.: Mortality of Acute Appendicitis. ANNALS OF SURGERY, **103,** No. 3, 362–374, March, 1936.

[8] Marchini, F.: L'abolizione del drenaggio nelle peritoniti purulente circoscrette e diffuse, specialmente da appendicite. (Abolition of Drainage in Circumscribed and Diffuse Peritonitis, Especially from Appendicitis.) Arch. ital. di chir., **28,** 549, 1931. (Abst. Surg., Gynec. and Obstet., **53,** 330–331, October, 1931.)

POLYCYSTIC DISEASE OF THE PANCREAS (DYSONTOGENETIC CYSTS)

REPORT OF A CASE WITH PARTIAL PANCREATECTOMY

K. K. NYGAARD,* M.D.,
FELLOW IN SURGERY, THE MAYO FOUNDATION
AND
WALTMAN WALTERS, M.D.
DIVISION OF SURGERY, THE MAYO CLINIC
ROCHESTER, MINN.

CYSTS of the pancreas may be considered comparatively rare. This condition most frequently presents interesting points as regards the clinical diagnosis or the pathologic picture found at exploration or at necropsy as well as ample reason for wondering as to the possible etiology and pathogenesis.

Schmieden and Sebening,[3] in 1927, reported 128 cases in which operations were performed for cysts of the pancreas. In 73 cases the origin of the cysts was not known, in 16 the cysts originated from previous trauma, in 28 they occurred following acute disease of the pancreas, and in 11 they were found in a tumor of the pancreas. According to Robson and Moynihan,[2] pancreatic cysts may be classified as follows: (1) Retention cysts; (2) proliferative cysts, cystic adenoma, and cystic epitheliomata; (3) hydatid cysts; (4) congenital cysts; (5) hemorrhagic cysts; and (6) pseudocysts.

Rarest among these cysts are the congenital cysts of the pancreas, which for the sake of description have been termed "polycystic disease of the pancreas." Pathologists have used the term "dysontogenetic cysts of the pancreas," which is a better term than "polycystic disease of the pancreas." It is a known fact that this type of cyst frequently occurs with other cysts, especially cysts of the kidneys, liver, and central nervous system. This association suggests a definite etiologic relationship between these different cysts. Lindau,[1] in his classic monograph on this subject, has furnished a new understanding of the pathologic picture of hemangiomata of the central nervous system and their relation to dysontogenetic cysts of the pancreas and kidney. In addition to five cases which he observed personally, Lindau collected ten cases from the literature. Dysontogenetic cysts of the pancreas were present in eight, cysts of the kidneys were present in ten, hypernephromata were present in six, and tumors of the suprarenal glands were present in two of these 15 cases. At the present time in the files of The Mayo Clinic there are histories of four cases presenting this syndrome, which in the recent literature has been described as "Lindau's disease." These cases will be reported later.

In the present communication we wish to present a case of dysontogenetic

* Now residing in Oslo, Norway. Submitted for publication January 7, 1937.

cysts of the pancreas in which there was no clinical indication of any lesion of the central nervous system. From the scattered reports in the literature it is very difficult to get a definite idea as to the frequency with which a polycystic disease of the pancreas is found without simultaneous lesions of the central nervous system. This case, however, will illustrate the necessity of ruling out such a possible combination. When the patient entered the clinic the symptoms predominantly were referable to the abdomen.

Case Report.—A woman, age 39, registered at the clinic February 12, 1936, because of abdominal pain. Her family history was essentially negative. She had been married 21 years and had had two children. The patient had never been very strong, but had always worked hard. Since 1934 she had felt much weaker than previously. About September, 1933, she first had noted a slight soreness in the left side of the abdomen when carrying anything heavy. This soreness had disappeared when she had rested or had assumed the recumbent position. Six months later she accidentally had felt a hard lump in the upper left side of her abdomen. She had noted that this palpable tumor had been gradually getting larger, and that the abdominal soreness had increased moderately. About February, 1935, she had detected a similar tumor in the upper right quadrant of her abdomen. This tumor had been growing more rapidly than the one on the left side, especially during the last two months before the patient came to the clinic. There had been an associated soreness on the right side, which had been of a pinching character. During 1935 she had had a constant sensation of abdominal fullness and an occasional attack of nausea, but she had not vomited. Her appetite had remained good except for the last three weeks before she came to the clinic. There had been some shortness of breath and she had been cold and restless most of the time. During 1934 and 1935 she had lost about 14 pounds (6.4 Kg.). Since 1921 the patient had had "rheumatism," especially in both arms, in the back of her neck, and in the small of her back. During 1935 the "rheumatic" pains in her arms had been associated with a rather marked numbness of both hands and arms, which had been aggravated by the occasional pains in her back. There had not been any marked headache, any dizziness, or any visual disturbances.

Physical Examination.—The patient was in general good physical condition. Blood pressure 112/80. The abdomen appeared to be moderately distended. Palpation revealed a large, irregular, somewhat hard mass, the size of a grapefruit, in the left upper quadrant. Palpation of the right upper quadrant revealed a similar mass which was slightly larger. The tumors moved with respiration and when the patient changed her position. Photo-electric estimation of the hemoglobin was 13.6 Gm. R.B.C. 4,150,000, W.B.C. 9,100. The urine was normal.

Roentgenologic Examination.—The thorax and colon were normal. There were slight hypertrophic changes in the lumbar vertebrae. An intravenous urogram, which was made in order to exclude the possibility of a polycystic kidney, revealed a ptosis of the right kidney and an extrarenal shadow below and adjacent to the lower pole of the left kidney. The origin and the nature of the palpable masses were still not entirely clear. The impression remained that this might be a case of either a mesenteric or a pancreatic cyst. A retroperitoneal tumor was not thought likely because of the rather free mobility of the masses.

Operation.—An exploratory laparotomy was performed (W. W.) February 2, 1936. The kidneys and liver were normal and did not contain any cysts. The entire pancreas was filled with cysts which varied from one to three centimeters in diameter. The two masses felt in the upper quadrants of the abdomen were groups of cysts which contained colloidal material. A resection of the lateral fourth of the pancreas was carried out, and a mass of cystic and colloid material 10 to 12 cm. in diameter was removed. The remaining fourth of the pancreas, the tail, was sutured to the proximal two-fourths. The

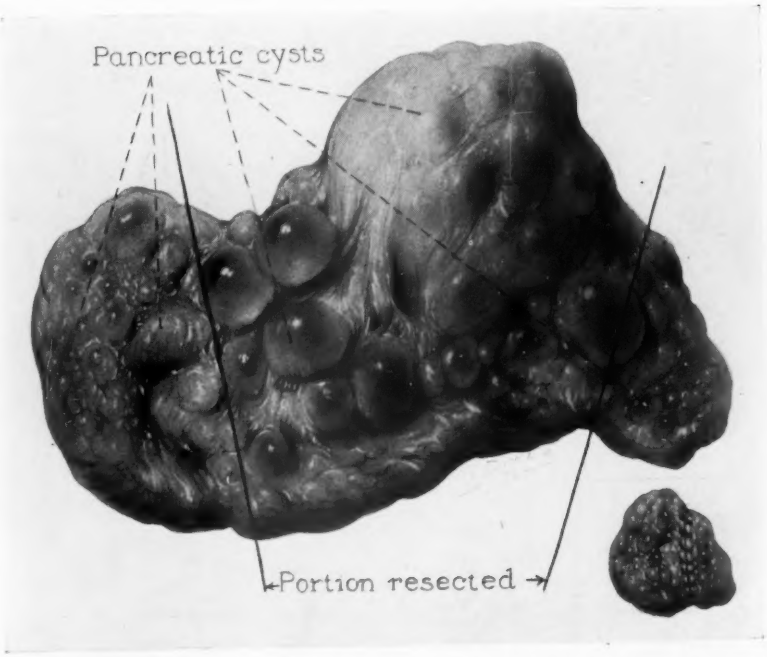


FIG. 1.—Drawing of the pancreas as seen at operation, showing the general involvement by multiple small and larger cysts. The part of the pancreas lying between oblique lines was resected. Insert shows continuity of pancreas which was effected after resection of its middle part.

FIG. 2.—Photograph of the part of the pancreas resected.

head of the pancreas was also polycystic but, because of the anatomic relationship to important neighboring organs, the cysts (Figs. 1 and 2) in this part of the pancreas were not removed.

Microscopic Examination revealed small and large cysts filled with a hyaline substance. The walls were covered by one layer of cuboidal epithelium; at certain places the epithelium was cylindrical in character. At other places these epithelial cells formed papillary proliferations which extended into the lumen of the cysts (Fig. 3). Very few islands of Langerhans were observed.

Postoperative Course.—Following the operation the patient made an uneventful recovery. The diastase in the urine was determined daily following the operation, but at no time was there any definite increase of it. On the fourteenth postoperative day a

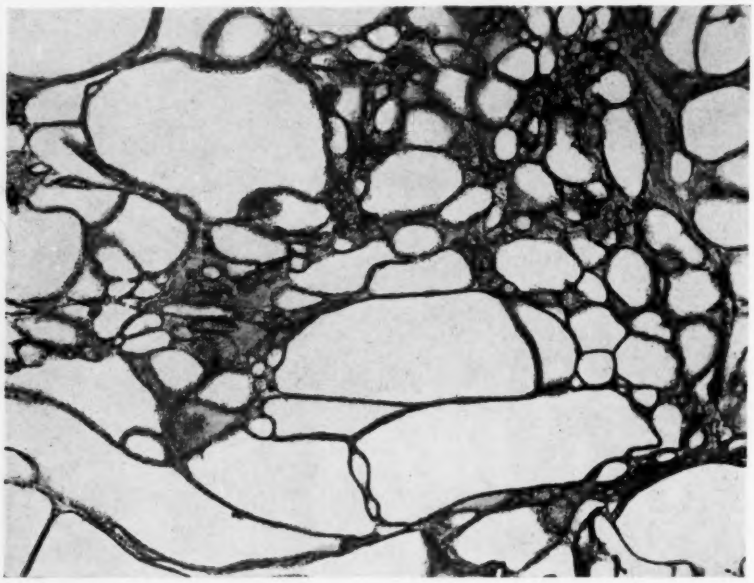


FIG. 3.—Photomicrograph showing small and large cysts, the walls of which are lined by a layer of cuboidal epithelium which forms papillary proliferations at certain points (×30).

glucose tolerance test was moderately positive and a restriction of her carbohydrate intake was advised. At the time of her dismissal, March 7, 1936, her general condition was excellent. The palpable tumor in the right upper abdominal quadrant was found to be definitely reduced in size; it was as large as a good-sized plum. The patient was advised to return to the clinic for a reëxamination after a few months.

Follow Up.—August 13, 1936: Since the operation her general condition has been satisfactory. The soreness in the right upper quadrant, which was noted before the operation, was still present, but no soreness was noted on the left side. The tumor in the right upper quadrant had not increased in size since her discharge. The examination otherwise was essentially negative. The blood sugar was normal. Because of the particular type of cysts of pancreas which had been present, it was deemed very important to rule out the possibility of Lindau's disease. A careful neurologic examination was undertaken. This included an examination of the eyes and ocular fundi. No disease of the central nervous system was present. This excluded the possibility of Lindau's disease.

COMMENT.—From a diagnostic point of view, this case presented to the clinician most of the difficulties associated with obscure tumors of the ab-

dominal cavity. It demonstrates very well that an approach to a tentative diagnosis can only be made by the application of all diagnostic skill. The value, for instance, of the excretory urogram in this case is obvious as it eliminated the possibility of polycystic kidneys. The resection of the pancreas was rather extensive. It is interesting to note that in spite of this the amount of urinary diastase did not increase postoperatively beyond normal limits. Another interesting fact was the moderately positive glucose tolerance test two weeks after the operation. In regard to the comparatively few islands of Langerhans found in the removed specimen, it may be assumed that the resected portion did not include a very active part of the pancreas, and that sufficient islands of Langerhans remained to enable the body to carry on a comparatively normal carbohydrate metabolism. Lindau mentioned that cysts of the pancreas were found in eight of 15 cases of Lindau's disease. In only two cases was there evidence of glycosuria.

The ultimate fate of the patient in the present case is doubtful. The pathologic condition must be considered congenital and the lesion no doubt required years to reach its preoperative size. It is a question whether or not this patient has reached a period of very active growth of the cysts, as seems indicated by the clinical history. Another possibility which warrants a guarded prognosis in this case is the possibility of future involvement of the central nervous system. Although at the present we have no experience as regards this possibility, it seems at least theoretically possible that the abdominal symptoms may precede the neurologic symptoms, which would make the ultimate prognosis unfavorable.

REFERENCES

[1] Lindau, Arvid: Studien über Kleinhirncysten bau, Pathogenese und Beziehungen zur Angiomatosis Retinae. Acta. path. et microbiol. Scandin., Suppl., **1**, 1–128, 1926.

[2] Robson and Moynihan: Quoted by Stillman, Alfred: Surgery of the Pancreas at the Roosevelt Hospital from 1918 to 1928. ANNALS OF SURGERY, **90**, 58–64, July, 1929.

[3] Schmieden, V., and Sebening, W.: III. Chirurgie des Pankreas. Arch. f. klin. Chir., **148**, 319–387, 1927.

CULLEN'S SIGN IN ACUTE PANCREATITIS

LAWRENCE S. FALLIS, M.D.

DETROIT, MICH.

FROM THE DEPARTMENT OF SURGERY, HENRY FORD HOSPITAL, DETROIT, MICH.

SINCE Cullen,[3, 4] in 1919, described the occurrence of discoloration of the skin around the umbilicus, it has been noted in conditions other than ruptured ectopic gestation. The association of this sign with acute pancreatitis has been recorded by Grey-Turner[6] in England, in 1920, two cases; by Johnson[7] in America, in 1930, one case; and by Petrivalsky[9] in Germany, in 1931, who in addition to three cases of his own cites a case report by Stutzer.[12] To these seven cases three additional instances are herewith added.

Case 1.—A female, age 68, was admitted to the Henry Ford Hospital, July 14, 1932, with a complaint of severe abdominal pain, which had had its onset two days previously following an attack of vomiting. The pain which had been constant and very severe was located in the right upper quadrant of the abdomen and radiated to the back beneath the angle of the right scapula.

Past History.—For the past two years, she had had similar but less severe attacks of right upper quadrant pain, intermittent in character, lasting about two days. On one occasion there had been slight jaundice present. For a number of years, she had complained of gaseous eructations.

Physical Examination.—Patient resting quietly. Temperature, 101° F.; pulse, 120; W.B.C., 14,000; polys., 86 per cent. Abdomen slightly distended. Not a great deal of muscle spasm; definite tenderness in midepigastrium. A diagnosis of acute cholecystitis was made and conservative treatment advised. The following day, that is three days after onset, a discoloration was noted in the skin around the umbilicus. On the basis of a positive Cullen's sign a diagnosis of acute pancreatitis was made and operation advised.

Operation.—July 15, 1932. Under spinal anesthesia the abdomen was opened through a midline incision above the umbilicus. The peritoneal cavity contained a large amount of blood stained fluid, which was removed by suction. Numerous areas of fat necrosis were observed in the omentum and mesocolon. Access to the lesser peritoneal cavity was effected through the gastrocolic omentum and contained much blood stained fluid. An engorged pancreas was palpated. The gallbladder was not distended and was free of gallstones. The lesser peritoneal cavity was drained with three cigarette drains and the abdomen closed. Death ensued six hours later.

Case 2.—A female, age 64, was admitted to the Henry Ford Hospital, December 4, 1935, complaining of abdominal pain, which had begun six days previously with vomiting at its onset. It was located in the epigastric region and had been continuous with acute exacerbations requiring morphia for relief. The epigastric distention was relieved by vomiting which occurred after the taking of food or drink. *Past History.*—The patient had complained of gas on stomach for the past five years. She had had several attacks of severe abdominal pain during this period. No history of jaundice.

Examination.—An acutely ill and obviously uncomfortable patient. Temperature, 96° F.; pulse, 112; W.B.C., 14,300; polys. 90 per cent. Blood sugar 154 mg. Diastatic activity 42. Slight icteric tint to skin. The abdomen is not distended; slightly tender on pressure over gallbladder, moderately tender in epigastrium and very tender

Submitted for publication October 26, 1936.

over left upper quadrant. In the latter region there was a hard irregular mass extending from the rib margin down toward the crest of the ilium. Diverticulitis with abscess formation was considered to be the most probable diagnosis. The patient's general condition improved sufficiently to permit abdominal exploration. When the abdomen was exposed to the strong light of the operating room, a yellowish discoloration of the skin around the umbilicus and a similar area of discoloration in the left flank was noted. A last minute preoperative diagnosis of acute pancreatitis was made on the basis of a positive Cullen's sign.

Operation.—December 6, 1935, the abdomen was opened through an upper left rectus incision under local infiltration with novocain. There was no blood stained fluid found in the peritoneal cavity. The omentum, showing evidence of fat necrosis, was found in the left upper quadrant surrounding an area of hemorrhage and induration between the layers of the left half of the mesocolon. The lesser peritoneal cavity was explored through the gastrocolic omentum. The tail of the pancreas was found to be engorged but no free fluid or pus was seen. Cigarette drains were introduced into the lesser sac and the abdomen closed. The gallbladder was distended. An upper right transrectus incision was made under local anesthesia and a cholecystostomy performed. The gallbladder did not contain stones. The patient recovered.

Case 3.—A male, age 48, was admitted to the Henry Ford Hospital, February 21, 1936, for treatment of a mass in the abdomen. Nine days previous to admission he had been seized with a sudden, severe attack of nausea and vomiting followed by profuse perspiration and a sensation of profound weakness. There was no abdominal pain. On February 20, he was seized with a sudden severe prostrating pain in the left upper quadrant. During the evening, the pain subsided but he was awakened at 4 A.M. by a return of the pain and at that time he noticed a lump in the left upper quadrant of the abdomen.

Past History.—One year previously he had been admitted to the hospital for observation, following an attack of severe upper abdominal pain. The pain was in the right upper quadrant and radiated around to the right scapular region. There had been several similar attacks and on one occasion he had been jaundiced. There was a history of glycosuria at intervals.

Physical Examination.—Patient lying comfortably in bed. Temperature, 100.2° F.; pulse, 78; blood sugar, 105. Benedict's test negative. Abdomen not distended. No muscle spasm. In the left upper quadrant, on palpation there was felt a rounded mass four inches in diameter. The lower limit of the mass was at the level of the umbilicus. It was slightly tender. There was a yellowish tint to the skin about the umbilicus for a distance of one inch. On the basis of a positive Cullen's sign, a diagnosis of acute pancreatitis was made.

Operation.—February 25, 1936, under ethylene and ether anesthesia, the abdomen was opened through a left rectus incision. There was no free fluid and no evidence of fat necrosis noted in the peritoneal cavity. The mass consisted of hemorrhage and edema in the left half of the transverse mesocolon. The lesser peritoneal cavity was entered through the gastrocolic omentum and was found to contain a little blood stained fluid. The body of the pancreas toward the left was edematous and the tail of the pancreas was greatly indurated. The inferior leaf of the transverse mesocolon was incised and blood stained hemorrhagic secretion and pancreatic tissue were evacuated. Cigarette drains were placed to the area through a stab wound at the costal margin. The gallbladder was not drained inasmuch as it was not distended and did not contain stones. Recovery was uneventful.

COMMENT.—Cullen, in 1918, was the first to recognize the importance of the sign and to make use of it in arriving at a correct preoperative diagnosis, though Hofstatter, in 1909, made the first report of the sign. In England it is known as Grey-Turner's sign, as he was the first to reports its diagnostic

value in acute pancreatitis. There appear to have been two conditions described under the heading of Cullen's sign; one in which intraperitoneal blood is seen shining through the tissues of a thin umbilicus. This same observation has been made in cases of umbilical, postoperative ventral, and femoral herniae, and is clearly due to intraperitoneal hemorrhage or hemorrhage into a structure in intimate contact with the hernial sac, as for example a strangulated portion of omentum. The other condition is that in which there is discoloration of the subcutaneous tissues around the umbilicus or even at some distance from it, as occurred in one of Grey-Turner's cases and as noted in Case 2. The discoloration suggests extravasation of blood in the subcutaneous tissue and further resembles ecchymosis in that the color is at first a bluish-black, fading through greenish and finally yellowish tints before disappearing. Since this description answers that originally communicated by Cullen, I agree with Smith and Wright[10] that it would be better to confine the use of the term "Cullen's sign" to those cases in which there is an actual discoloration of the skin. There is no unanimity of opinion among observers as to the exact nature of this phenomenon. If we exclude cases in which the blood is seen shining through the umbilicus, the favored explanation would seem to have a lymphatic basis, inasmuch as there is a rich anastomosis between the lymphatics of the subcutaneous tissues and those of the peritoneum and subperitoneal tissues. Petrivalsky, in support of this theory, has shown by a series of experiments that if the omentum is adherent elsewhere or so short that it does not reach the umbilicus, thus permitting intraperitoneal blood to be in actual contact with the anterior abdominal wall, discoloration will result. The extreme rarity of the sign suggests an anatomic variation of the structures at the umbilicus. Abnormal apertures in the peritoneum and fascia transversalis would allow extravasation of blood from the peritoneal cavity to the subcutaneous tissues. Another explanation is that the blood travels extraperitoneally. This hypothesis is all the more plausible when it is recalled that the pancreas is essentially an extraperitoneal organ, lying as it does behind the peritoneum and being covered by peritoneum only on its anterior surface. Effusions of blood resulting from disintegration of the gland could conceivably track around in the subperitoneal space between the peritoneum and transversalis fascia and reaching the midline anteriorly would be limited by the suspensory ligament of the liver above, and the urachus below the umbilicus. Collections of fluid would then tend to gravitate along these structures and pool in the potential subumbilical space where there is direct contact with the subcutaneous tissues owing to the absence of the transversalis fascia in this region. Diffusion of excess fluid into the flank would readily occur from here.

We offer in confirmation of this postulate, the observation that in Cases 2 and 3 there was no blood stained peritoneal fluid found at operation and yet a positive Cullen's sign was present, while in two other cases of acute pancreatitis under consideration at the same time, there was found at operation, in both instances, a large amount of blood stained peritoneal fluid but no discoloration around the umbilicus.

The theory of extraperitoneal spread is also applicable to cases of ruptured ectopic gestation and may explain the rarity of the sign. On this basis, however, the sign would be positive only in those cases in which the extraperitoneal portion of the tube was involved in the rupture and extravasation took place between the layers of the broad ligament.

The diagnosis of acute pancreatitis is difficult and in spite of Moynihan's[8] admonition that it is not diagnosed because the surgeon is not thinking of this condition, a preoperative diagnosis is infrequently made. In a series of 35 cases operated upon for acute pancreatitis in this hospital, a positive diagnosis was made in only five instances and, of these, one had suffered from a previous attack of acute pancreatitis. The diagnostic value of a positive Cullen's sign is emphasized by pointing out that of the remaining four cases in which a correct preoperative diagnosis was made, three of them were made on a basis of a positive Cullen's sign. A good light is essential for the recognition of the sign and doubtless in many instances the observation has not been made because of poor illumination. In one of our cases and in a case reported by Smith and Wright, the discoloration was not recognized until the patient's abdomen was exposed to the strong operating room light.

SUMMARY.—(1) Three cases of a positive Cullen's sign in acute pancreatitis are presented.

(2) The mechanism of spread of the blood to the subcutaneous tissue is discussed.

(3) The extreme rarity of the sign is noted.

(4) The diagnostic value of the sign is stressed.

REFERENCES

[1] Bailey, H.: Clinical Aspects of Acute Pancreatitis. Brit. Med. Jour., **1**, 367–369, February 26, 1927.

[2] Cope, Z.: Early Diagnosis of the Acute Abdomen, 2nd ed. London, Henry Frowde and Hodder and Stoughton, 1923.

[3] Cullen, T. S.: Contributions to Medical and Biological Research (dedicated to Sir William Osler). Am. Jour. Obst. and Gynec., **78**, 457, 1918.

[4] Cullen, T. S.: Embryology Anatomy and Diseases of the Umbilicus. Philadelphia, W. B. Saunders, 1916.

[5] Cunningham, D. J.: Textbook of Anatomy, ed. by Arthur Robinson, 5th ed. rev., New York, William Wood & Co., 1923.

[6] Turner, G. G.: Local Discoloration of the Abdominal Wall as a Sign of Acute Pancreatitis. Brit. Jour. Surg., **7**, 394–395, January, 1920.

[7] Johnson, L. B.: Acute Hemorrhagic Pancreatitis: A Case Presenting Yellow Discoloration at the Umbilicus. J.A.M.A., **95**, 1587–1588, November 22, 1930.

[8] Moynihan, Sir B.: Acute Pancreatitis. ANNALS OF SURGERY, **81**, 132–142, January, 1925.

[9] Petrivalsky, Julius: Versuche zur Aufklärung des Grundwesens der Verfärbung der vordered Bauchwand bei akuter Pankreasnekrose sowie auch bei geplatzter extrauteriner Gravidität. Zentralbl. f. Chir., **58**, 3013, 1931.

[10] Smith, I., and Wright, F. J.: Cullen's Sign in Ruptured Gestation: Report of Two Cases. Lancet, **1**, 930–932, April 20, 1935.

[11] Stabler, F.: Case Showing Cullen's Sign. Brit. Med. Jour., **2**, 255–256, August 11, 1934.

[12] Stutzer, E.: Ein Beitrag zur Feststellung der Bauchspeicheld-rüsenapoplexie. Zentralbl. f. Chir., **58**, 597, 1931.

"LIVER DEATHS" IN GENERAL SURGERY

TWO CASES UNASSOCIATED WITH BILIARY TRACT OPERATIONS

JOSEPH L. DECOURCY, M.D.

CINCINNATI, OHIO

FROM THE DEPARTMENT OF SURGERY, DE COURCY CLINIC, CINCINNATI, OHIO

THE term "liver death" was first applied to fatalities occurring after operations upon the biliary tract when the operation was followed by a rapid rise in temperature without any evidence of infection and death occurred within two or three days.

In these cases there was no jaundice or other clinical evidence of severe liver damage, yet it is generally recognized that there is some degree of hepatitis usually associated with gallbladder disease. Hence these sudden "high temperature" deaths have been attributed to toxemia resulting from further damage to the liver by operation. Recently it has been recognized that a similar type of hyperpyrexial death without evident cause may follow operations other than those upon the biliary system.

In 1934, Connell,[1] who in an earlier article (1931) had stated that review of the postoperative records of laparotomies showed no similar syndrome in other than biliary tract operations, reversed this opinion. He reported five instances of "high temperature" deaths occurring after other intra-abdominal procedures. In two of these cases, the syndrome followed simple interval appendicectomies for chronic appendicitis. The three other cases were repair of a ventral hernia, removal of an ovarian cyst, and an hysterectomy (with appendicectomy).

At the New Orleans Charity Hospital[2] a syndrome showing "a striking parallelism" to that of "liver death" in gallbladder surgery has been observed, following not only other abdominal operations but also extensive burns. Commenting on these findings, Boyce[3] states that "as interest in this type of death has increased, there has been an increasing feeling that the syndrome is not confined to biliary surgery, but occurs, and not infrequently, in other postoperative conditions." Two cases recently seen in my own clinic presented this same syndrome after abdominal operations which did not involve the biliary tract.

CASE REPORTS

Case 1.—The patient was a male, age 59, upon whom a colostomy was performed, following careful preparation, as the first stage of a removal of the rectum for carcinoma. He had lost considerable blood with a resulting secondary anemia of 2,850,000 red blood cells. A transfusion was given several days before operation, with no reaction, and no glucose was administered.

Within 24 hours after operation the temperature rose to 106° F. per rectum and remained at this level until death, which occurred 72 hours later. No cause for the hyperpyrexia was discovered. The chest and abdominal findings were entirely negative.

Autopsy.—A complete postmortem examination with the exception of the head revealed

Submitted for publication September 15, 1936.

no cause of death. There was a plastic exudate about the distal portion of the inverted sigmoid with no evidence of infection or localized peritonitis.

Microscopic Examination.—The liver showed some fat necrosis (this was apparent grossly also). There was also evidence of perihepatitis along the edge of the liver near the gallbladder, but no evidence of cholecystic disease. Thyroid appeared normal.

Case 2.—The patient was a female, who had lost considerable blood from a submucous fibroid and was quite anemic. A transfusion was given before operation without reaction.

The temperature rose to 107° F. per rectum within 24 hours after an hysterectomy had been performed and remained at that level, in spite of treatment, until death, 48 hours later. As in Case 1 no cause could be found for the hyperpyrexia. There was no evidence of peritonitis or ileus, and all findings were negative.

Autopsy.—The pelvic peritoneum showed what might be termed a low grade chemical peritonitis. No pus was found. There was plastic exudate over suture lines. The remaining portion of the peritoneal cavity was normal in appearance. Examination of head was not made. Thyroid appeared normal.

Pathologic Examination, Gross.—Liver was pale with cut surface showing some fat necrosis. *Microscopic* evidence of liver necrosis.

In some cases high temperatures occurring postoperatively have been attributed to a toxic action on the thermal center, as is frequently seen following thyroidectomies for hyperthyroidism in patients not properly prepared. But in the "high temperature" deaths that follow biliary tract operations, the clinical picture indicates "an overwhelming toxemia" (Eiss[4]), which has been attributed to liver damage, because evidence of liver involvement is so frequently associated with gallbladder and biliary tract disease and operation would unavoidably increase such damage.

In a recent article Sharples[5] draws an interesting comparison between the terminal pyrexia of uremia and the hyperpyrexia characteristic of "liver death." "In each there is a more or less gradual cessation of function," he says, "and in each if this function suddenly ceases, producing analogous symptoms, death follows." But the kidney has only one function, that of excretion, while the liver has many functions "in preparing the substances coming through the portal vein for use by the tissues of the body"; so that if all these functions are "suspended at once, the effect is more dramatic" than if kidney function alone is interrupted.

It is true that in these cases of so called "liver death" definite pathologic changes have not always been found in the liver. In some cases of gallbladder disease, the changes are demonstrable in the liver; but they are the same as are found by biopsy at the time of operation. Others, however, have found a focal necrosis in the liver as a rule in cases of "liver death" (Boyce,[3] Sutton[6]). In most of the cases reported by Boyce and McFetridge,[2] in which the typical "high temperature" death occurred, necrotic changes were found in the liver, whether there was biliary tract disease or not. Of the five cases reported by Connell[1] in operations other than on the biliary tract, no autopsy was performed in two cases; in two others the autopsy failed to show any cause of death; in one (hysterectomy) there was fat necrosis of the liver.

Admitting that some damage to the liver is the cause of the toxemia, hyperpyrexia and death in the type of case under discussion, the mechanism by which this toxemia is produced is still obscure. The liver is known to have

many important functions, among them a *detoxifying function.* Is the toxemia due to a sudden cessation of this function, allowing toxic substances to be poured into the blood stream (as suggested by Sharples)? Or do the damaged liver cells themselves produce some toxic substance? These are questions which are not yet solved and which await our further investigation.

"Liver deaths," as has been noted, occur most frequently in biliary tract disease, in which the liver usually shows some pathologic changes at the time of operation. But hepatic damage may be present in other cases due to infection, intestinal intoxication or, I believe, anemia. If it is present, even to a slight degree, any laparotomy may cause "physical, chemical, infectious, mechanical and toxemic traumata" (Heyd[7]) sufficient to produce severe toxemia when liver function is impaired.

In the two cases herewith cited, the only factor common to them both was a considerable degree of prolonged anemia resulting from preoperative blood loss. I do not find this point especially noted by others reporting "high temperature" deaths after abdominal operations. Connell reports postoperative hemoglobin determinations in four of his cases, in three of which the hemoglobin was below 75 per cent and in two instances 60 and 65 per cent respectively. In two cases in which postoperative red cell counts were made, the red cells were below normal in one (3,700,000). I would like to suggest the possibility, however, that the diminished or poor blood supply to the liver resulting from anemia may be the cause of preoperative damage to the liver cells or of some diminution of the liver function.

In a recent series of experiments on dogs in which cholecystectomy was performed, Sutton[6] ligated the hepatic arteries; 6 of the 11 animals so treated developed the typical syndrome of high temperature and died within 36 hours. In the animals not developing this syndrome, it was found, by means of bismuth or starch mixture injections, that adequate collateral circulation to all the lobes of the liver had been established. In the animals dying with hyperpyrexia, autopsy showed focal necrosis of the liver similar to that seen in autopsies in human "liver deaths."

Sutton suggests that "liver death" results if "the liver is deprived of sufficient arterial blood" at the time of operation. Clinically he notes that arterial occlusion may be due to thrombosis, embolism or accidental ligation. But a prolonged anemia might also interfere with adequate arterial blood supply and thus cause damage to the liver cells that would be intensified by any operation to the point of causing "liver death."

Even in biliary tract surgery "liver deaths" do not occur in jaundiced patients or those with clinical symptoms of liver disease, but rather in patients that appear to be good surgical risks. It would be most desirable if we could determine before operation what patients have even the slightest degree of liver dysfunction and are consequently in danger of further liver damage from operative procedures.

Many tests of liver function have been described and many are in use in the study of diseases of the liver and in the preoperative study of patients

with gallbladder disease. In fact, Graham[8] states that his dye retention test was developed on the basis of his findings in four cases of "liver death." The dye used in this test (isoiodeikon) had been given these patients intravenously for cholecystography prior to operation, and a study of the records showed a high retention of the dye in each case. Yet even the dye retention tests are not satisfactory indicators of the whole function of the liver and cannot be relied upon to show the slighter degrees of damage or dysfunction, which may nevertheless be a source of danger to the surgical patient.

It has been shown both experimentally and clinically that building up the glycogen reserves of the liver protects it from damage and increases its detoxifying action. This is best effected by the administration of glucose preoperatively. This procedure has reduced the incidence of "liver deaths" in gallbladder surgery, and is used as a routine in our clinic before all biliary operations. Both Connell[1] and Heyd[9] suggest the preoperative administration of glucose in other operations as well; the latter is of the opinion that it should be used in all laparotomies.

Since my own experience leads me to believe that anemia may be a factor in the causation of liver damage, I should certainly recommend that glucose be given preoperatively, as an adjunct to transfusion, to all patients who show any evidence of anemia.

SUMMARY.—Two hyperpyrexial fatalities of a type resembling "liver death," but occurring apart from biliary tract operations, are reported. One operation was a colostomy for carcinoma of the rectum; the other, a hysterectomy. In both cases autopsy failed to show the cause of death. Both patients showed a considerable degree of secondary anemia. Preventive measures are recommended.

CONCLUSION

It is suggested that anemia or deficient hepatic blood supply, aggravated by any abdominal operation, may be a factor in the causation of "liver death."

REFERENCES

[1] Connell, F. G.: Liver Deaths (So-Called); Rapid High Temperature Deaths. ANNALS OF SURGERY, **100**, 319, 1934.

[2] Boyce, F. F., and McFetridge, E. M.: So-Called "Liver Death"; Clinical and Experimental study. Arch. Surg., **31**, 105, 1935.

[3] Boyce, F. F.: The So-Called Liver Death Syndrome in Surgery. Surg., Gynec. and Obstet., **61**, 122, 1935.

[4] Eiss, S.: Conservation of Hepatic Function in Gall-Bladder Operations; Precautionary Measures to Prevent "Liver Deaths." ANNALS OF SURGERY, **98**, 348, 1933.

[5] Sharples, C. W.: Liver Deaths Following Operation of Biliary Tract. West. Jour. Surg., **42**, 337, 1934.

[6] Sutton, J. E., Jr.: High Temperature Liver Death Syndrome. Proc. Soc. Exper. Biol. and Med., **32**, 712, 1935.

[7] Heyd, C. G.: Protective Rôle of Liver in Abdominal Surgery. Am. Jour. Obstet. and Gynec., **19**, 203, 1930.

[8] Graham, E. A.: Lowering Mortality after Operations on Biliary Tract. Illinois Med. Jour., **60**, 196, 1931.

[9] Heyd, C. G.: Chemical Mechanism of Liver Protection in Abdominal Surgery. Am. Jour. Obstet. and Gynec., **27**, 366, 1934.

THE FALSE "ACUTE ABDOMEN"

I. PSEUDOPERFORATION OF PEPTIC ULCER

THEODORE L. ALTHAUSEN, M.D.

SAN FRANCISCO, CALIF.

FROM THE DEPARTMENT OF MEDICINE, UNIVERSITY OF CALIFORNIA MEDICAL SCHOOL, SAN FRANCISCO, CALIF.

PERFORATION of peptic ulcers with mild or atypical symptoms is not uncommon. On the other hand, a clinical picture of perforation without any pathologic findings at operation is rare, judging by a review of the medical literature for the past 20 years. Interest in the following cases is enhanced by the fact that both patients were in the hospital undergoing treatment for peptic ulcer when symptoms and signs pointing to perforation developed.

Case 1.—A. A. S., a white female, age 48, who, following a period of financial worries, began to feel a dull, burning pain in the epigastrium six months before entry. This pain radiated to the back and was relieved by food. She was put on a milk diet with alkaline powders and obtained complete relief of her symptoms. Six weeks before admission epigastric pain returned, but was more severe. This time the Sippy regimen afforded only partial relief. She lost 6 Kg. in weight. Physical examination was negative except for moderate tenderness in the epigastrium. Blood counts, Wassermann and Kahn reactions, sedimentation rate, urine analysis, phenolsulphonephthalein test, examination of stools, and gastric analysis were negative. Gastro-intestinal series showed a wide ulcer crater on the posterior wall of the upper third of the stomach (Fig. 1). After six hours there was a 25 per cent residue with a barium fleck in the ulcer crater. Cholecystography was negative.

The patient was put on a strict Sippy regimen with tincture of belladonna. Her pain disappeared in two days but recurred on the sixth day and persisted in spite of treatment. On the seventh day she began vomiting, and the epigastric pain with radiation to the back became continuous and so severe that full doses of codeine gave little relief. Up to 3:45 P.M. on the eleventh day, the patient's abdomen was soft and the temperature normal. By 7:00 P.M. the abdomen had become rigid and very tender; the rectal temperature was 38.4° C.; there were 15,000 W.B.C. per cu. Mm. with 85 per cent P.M.N. The urine was negative. Two hours later she was operated upon by Dr. Leon Goldman for perforation of a gastric ulcer. He explored the stomach anteriorly and posteriorly after opening the gastrohepatic omentum, but found neither perforation nor ulcer. Complete exploration of the abdomen also gave no explanation of the clinical picture. After operation the pain disappeared and the patient made an uneventful recovery.

In an effort to find the cause of the attack, the following procedures were employed, all of which were negative: Lumbar puncture, tests for hematoporphyrin in the urine, plasma chlorides, and roentgenologic examination of the thoracic spine. Roentgenologic examination of the stomach revealed no evidence of the former ulcer. Six months after discharge, the patient reported no recurrence of any abdominal symptoms, and a gain in weight of 5 Kg.

Case 2.—P. W. H., a white male, age 46, was admitted to the hospital for hematemesis. For many years he had suffered at intervals from burning sensation in the epigastrium. In the past five years during which he suffered serious financial reverses, this burning discomfort had become a daily occurrence and was accompanied by local

Submitted for publication October 28, 1936.

tenderness. The burning often interrupted his sleep and was relieved by food or soda. A year and a half before entry he was seen in our Outpatient Department. An alcohol test meal showed 57 free HCl. A gastro-intestinal series demonstrated a 20 per cent gastric residue after seven hours, irritability of the first portion of the duodenum, and hypermotility of the lower intestinal tract. A Sippy regimen resulted in relief of symptoms. Four months before admission to the hospital, burning in the epigastrium recurred. During the week before entry, the patient had severe pharyngitis. On the morning before entry, following a cathartic, he passed three black watery stools and felt weak. Later that morning he suddenly vomited a large amount of mixed dark and bright red blood, and fainted. Since the recurrence of symptoms, the patient had lost 7 Kg. in weight. Physical examination showed a pale, weak man. Blood pressure 80/60. There was tender-

FIG. 1.—Roentgenogram showing an ulcer on the posterior wall of the upper third of the stomach in Case 1.

ness in the right epigastrium. Hb. 70 per cent (Sahli); R.B.C. 3,370,000 and W.B.C. 3,000, with a normal differential count; Wassermann and Kahn reactions negative. Stool: Black with three plus occult blood. Urine: Negative.

The patient was given the usual treatment for hemorrhage from peptic ulcer. On the day following admission, his temperature rose to 39.8° C. Abdominal tenderness became more marked, and spasticity appeared in the right upper quadrant. Daily W.B.C. counts ranged from 4,400 to 7,150, with normal differential counts. To explain the leukopenia in the presence of fever, the following tests were employed, all of which gave negative results: Urine culture; blood culture; agglutination for the typhoid-paratyphoid group, B. enteritidis, and the Brucella group; phagocytic index for the Brucella group; intradermal tuberculin tests. At this time a small perforation of the ulcer with leakage into the lesser peritoneal cavity was suspected. Soon after, the fever and other symptoms disappeared and the stools became negative for occult blood. On the fifteenth day, a gastro-intestinal series was attempted, but the patient fainted. About 4.00 P.M. on the same day, he began to have a dull pain along the costal margin

in the back, more marked on the right side and intensified by movement. Voluntary muscular spasm was found in the right upper quadrant. This pain became more severe after dinner and was aggravated by deep respiration. By 8:00 P.M. there was rigidity of the right upper quadrant; temperature 37.9° C.; W.B.C. 15,000. Fluoroscopic examination showed no free gas in the abdomen. The diaphragm moved freely, and the lungs were clear. At 11:00 P.M. the temperature was 38.3° C.; W.B.C. 18,000 with 92 per cent P.M.N.; and the urine negative. Three hours later, laparotomy was performed for probable perforation of a peptic ulcer.

At operation, Dr. Leon Goldman found no perforation and no ulcer, although the posterior wall of the stomach was explored digitally through an incision in the gastrocolic omentum. Careful exploration of the rest of the abdomen proved to be negative, also. The patient made a rapid recovery. Subsequent roentgenograms of the kidneys, ureters, and bladder were negative. The patient was observed for two years, during which time he had no acute attacks of pain but continued to suffer from a "sour stomach" for which he took soda.

DISCUSSION.—Presumptive diagnosis of peptic ulcer was made in both cases from the history. In the first case, roentgenologic examination showed a large gastric ulcer. In the second, the occurrence of a large hemorrhage without other known cause presented confirmatory evidence of the existence of a peptic ulcer. Failure to find an ulcer by exploration does not indicate that there was none 17 and 15 days, respectively, prior to operation. The rapidity with which peptic ulcers can heal under favorable conditions is well known. Moreover, the exploring surgeon may miss a small, or partly healed, ulcer unless the stomach is actually opened and its mucosa examined.

Symptoms and signs of an "acute abdomen" developed in both patients while on a Sippy regimen and were, at the time, interpreted as indicating a probable perforation of the ulcer. Since in neither patient perforation was found at operation, it is important to consider the clinical aspects, which in our cases differ from those of the classical picture. In an exhaustive study of the diagnosis of perforating peptic ulcer undertaken because "a large percentage of acute perforations do not reproduce the text-book picture and as a rule pass unrecognized," Singer[1] distinguishes three clinical stages of perforation. The preperforative stage consists of destruction of the gastroduodenal wall up to the serosa and is characterized by an increase in the intensity and refractoriness of the pain and the occurrence of vomiting. The stage of actual perforation, during which escape of gastric contents produces a chemical peritonitis, is typically recognized by sudden excruciating pain beginning in the epigastrium and spreading within a few minutes to the entire abdomen; the intensity of this pain depends to some extent on the amount of initial leakage. The postperforative stage is characterized by protective peritoneal and systemic reactions against the chemical irritation and the ensuing infection. During this stage the chemical picture is variable, but, in general, manifestations of sepsis progressively overshadow the element of pain.

The clinical manifestations in our patients were similar to those seen in the preperforative stage. However, there was absent the typical abrupt onset of extreme pain which, when present, permits the exact timing of the perforation, and the pain did not spread to the entire abdomen. Instead, pre-

existing symptoms were progressively aggravated, and indications of early sepsis suggested the beginning of the postperforative stage. A small perforation with slow leakage was thought at the time to account for the absence of the classical fulminating symptoms.

Turning to other possible causes of the acute clinical picture, a number of conditions were ruled out by surgical exploration, notably, acute appendicitis, acute cholecystitis, chronic cholecystic disease with complications (especially empyema or rupture of the gallbladder and biliary colic), acute pancreatitis, intestinal obstruction, diverticulitis of the sigmoid, Henoch's purpura, acute mesenteric adenitis, rupture of hepatic cyst, intestinal infarction, and torsion of the spleen or omentum. In the first patient, rupture of an ectopic gestation was likewise ruled out.

Diseases eliminated as improbable by the history, physical findings, laboratory data, or subsequent course were cardiac disease (especially coronary thrombosis, abdominal angina, and pericarditis), gastric crisis, lead colic, pulmonary disease (especially basal pneumonia and diaphragmatic pleurisy), diseases of the vertebral column (especially osteomyelitis and Pott's disease), arachnoidism, acute indigestion, acute Addison's disease, porphyrinuria (particularly in the first case) and ureteral colic (particularly in the second case).

There are two entities to be considered at greater length. One of these is diaphragmatic pleurodynia which may simulate an "acute surgical abdomen."[2] The possibility of pleurodynia is suggested in both patients under discussion, but especially in the second, by the prominence of pain along the costal margin and by the presence of fever, which is usually absent in the early stages of perforation. However, there are several objections to this diagnosis in our cases. In pleurodynia the leukocytes are within normal limits, whereas in our patients there was marked leukocytosis. In pleurodynia, the pain comes typically in paroxysms, lasting about 24 hours, with recurrences at intervals of 24 to 30 hours.[3] In contrast to this, our first patient complained of pain which became progressively worse for several days without periods of relief. Finally, the epidemiologic facts that pleurodynia often spreads by contact and affects children chiefly, also do not fit into the clinical picture of our patients.

The other possibility is abdominal allergy. Food allergy with violent symptoms which may be taken for an "acute abdomen" undoubtedly exists. A member of the faculty of our Medical School was operated upon for acute perforation of peptic ulcer with negative findings in the abdomen. The same individual had had a previous operation by the same surgeon for acute appendicitis, also without pathologic findings. Later, similar attacks were traced to sensitivity to eggs. Furthermore, symptoms of peptic ulcer, even to the occurrence of bleeding from the gastro-intestinal tract, may be simulated by abdominal allergy.[4]

In our cases abdominal allergy was not considered seriously enough even after operation to prompt a program of skin tests and elimination diets, because neither patient had ever had any cutaneous or respiratory manifesta-

tions of allergy. Also, eosinophilia was not present in either case. In addition, the first patient had her acute abdominal attack after having been on an exclusive diet of milk for 17 days, and probably should have had symptoms earlier if she had been sensitive to milk. She also tolerated well a milk diet six months previously. After operation these patients were followed for six months and two years, respectively, without recurrence of symptoms, on a general diet. In this connection it is of interest that prolonged freedom from bronchial asthma has been reported following anesthesia with ether.[5]

From this review, it is clear that even in retrospect a satisfactory diagnosis of the two reported cases cannot be made. It is interesting to consider two aspects of our cases which might have served to prevent operation. The first of these is the question of perforation in patients with peptic ulcer who are on a Sippy regimen. Hurst[6] writes that he has "never known an ulcer perforate when a patient was actually under treatment." Blackford and Baker[7] make an even more emphatic statement: "Acute perforation of peptic ulcer almost never occurs in a patient who has ever had any kind of advice for treatment of peptic ulcer, or any previous diagnosis of peptic ulcer." On the other hand, Vale and Cameron[8] reported five such cases over a period of 15 years. They found only two similar cases in the literature. At the University of California Hospital, a review of records obtained since Sippy described his treatment showed one patient with an acute, and one patient with a walled-off perforation of a duodenal ulcer that occurred while the patient was actually following the diet at home. From this it seems that perforation of a peptic ulcer under treatment is rare, but probably not so rare as a review of the literature would indicate.

In the second place, roentgenologic finding of free gas in the abdomen of patients suspected of perforation is very valuable confirmatory evidence. Finsterbusch and Grass[9] reported this finding in 86 per cent of 146 collected cases with perforation. Vaughan and Singer[10] found free abdominal gas in 85 per cent of 63 patients with classical symptoms, and in 70 to 75 per cent of all (97) cases. Unfortunately, as may be seen from these figures, the absence of free abdominal gas does not exclude perforation.

Since in our patients the clinical picture fell short of the fulminating perforation with shock, it may be asked why conservative treatment was not employed. Hurst,[6] among several other writers, advocates conservative treatment of the "subacute" or *forme fruste* type of perforation, which causes similar but less intense symptoms than those of "acute" perforation, and is not followed by signs of general peritonitis because spontaneous plugging of the leak usually takes place. However, my own experience and a review of records at the University of California Hospital show that it is impossible to segregate in advance perforations which become sealed spontaneously. For this reason I feel that if operation were to be withheld from patients having symptoms similar to those described in this paper, a certain number of acute perforations would be missed, with general peritonitis resulting. On the other hand, if the occurrence of a perforation in a given case of peptic ulcer is

doubtful, it is more justifiable to postpone operation when the patient has been for some time on a Sippy regimen; when there is no pneumoperitoneum; or when there is a history of allergic tendencies.

SUMMARY

(1) Two patients with peptic ulcer confirmed in one case by roentgenologic examination and in the other by the occurrence of hematemesis, while undergoing treatment in a hospital, developed symptoms and signs resembling perforation. Operation revealed nothing to account for the clinical picture in either case.

(2) The differential diagnosis of perforated peptic ulcer is discussed with special reference to diaphragmatic pleurodynia and gastro-intestinal allergy.

(3) The infrequent occurrence of perforation of peptic ulcer in patients on a Sippy regimen, and the high incidence of pneumoperitoneum in perforated peptic ulcer, are considered as possible aids in preventing useless operations.

(4) The danger of conservative treatment in the "subacute" type of perforated peptic ulcer is pointed out.

REFERENCES

[1] Singer, H. A.: The Diagnosis of Perforated Peptic Ulcer. International Clinics, **2**, 55; **3**, 116, 1935.

[2] Harder, F. K.: Epidemic Myalgia or Pleurodynia in Southwestern Ohio. Am. Jour. Med. Sci., **191**, 678, 1936.

[3] Welborn, M. B.: Epidemic Pleurodynia ("Devil's Grip") in Cincinnati. Am. Jour. Med. Sci., **191**, 673, 1936.

[4] Rowe, A. H.: Food Allergy. Lea and Febiger, Philadelphia, 1931.

[5] Kahn, I. S.: Surgical Anesthesia Deliberately Induced by Ether for the Semipermanent Relief of Chronic Intractable Bronchial Asthma. J. of Allergy, **6**, 556, 1935.

[6] Hurst, A. F., and Stewart, M. J.: Gastric and Duodenal Ulcer. Oxford University Press, London and New York, 1929.

[7] Blackford, J. M., and Baker, J. W.: Acute Perforating Peptic Ulcer. Am. Jour. Surg., **12**, 18, 1931.

[8] Vale, C. F., and Cameron, D. A.: Gastric and Duodenal Perforation During Hospital Treatment. ANNALS OF SURGERY, **103**, 353, 1936.

[9] Finsterbusch, R., and Grass, F.: Der Wert des frühzeitigen röntgenologischen Nachweises des spontanen Pneumoperitoneum bei perforientem Magengeschwür and sonstigen Erkrankungen des Verdauungstraktus. Acta Radiologica, **13**, 567, 1932.

[10] Vaughan, R. T., and Singer, H. A.: Further Observations on the Value of Radiology in the Diagnosis of Perforated Peptic Ulcer. Am. Jour. Surg., **21**, 392, 1933.

TUMORS OF THE RENAL PELVIS AND URETER *

JOHN R. CAULK, M.D.

ST. LOUIS, MO.

FROM THE DEPARTMENT OF SURGERY, WASHINGTON UNIVERSITY SCHOOL OF MEDICINE AND BARNES HOSPITAL, ST. LOUIS, MO.

BY REASON of: 1, Their rarity; 2, their inherent individual characteristics; 3, the diagnostic intricacies; and 4, surgical requirements, tumors of the renal pelvis have a significance sufficient to justify an intensive discussion before this association.

These growths are comparatively rare and comprise about 5 to 10 per cent of all renal tumors. The collected statistics of Albarran and Imbert, in 1903, showed 42 tumors of this variety in 585 cases of renal neoplasm. Scholl, in 273 cases, found 13 pelvic tumors. Out of 318 nephrectomies for renal tumor at the Mayo Clinic, Hunt states that 23 originated in the renal pelvis. Thomson-Walker has reported 15 per cent pelvic growths in 66 cases. Watson found one case of pelvic tumor in 98 cases. Meltzer's report is significant insofar as the records of the Massachusetts General Hospital during a period of 10 years disclose one case of the papillary type in 94 cases of renal tumor. Raddei has recorded 31 pelvic tumors in 435 cases. In 108 renal tumors, occurring in Barnes Hospital, seven tumors, or 6.5 per cent, were of the pelvic variety. Eighty-one of these tumors were removed; hence the proportion of pelvic tumors to those removed was 8.6 per cent. It is of interest to note that from 1910 to 1923 no case of primary tumor of the renal pelvis was recorded in our clinic. All seven cases occurred between 1923 and 1936, and five of these in the past two years.

Numerous papers have been published from time to time dealing with this subject; the majority of the authors have reported only one case which has usually been bolstered up by an extensive compilation of the literature. Appended to one of these reports, in 1925, there is a bibliography of 150 articles. And all told, the total number of cases which have been reported exceeds but slightly the number of authors in the bibliography.

Because of the rarity of these tumors, the surgeon is usually not as well informed as to their nature as he would be were rarity not their hallmark, and the consequence is that, as a rule, the operation prescribed is improper and misdirected. It is only through knowledge gained by an analytic study of a large series of collected cases that a thorough appreciation of the best methods of surgical therapy can be acquired.

With few exceptions these tumors are epithelial, the majority being of the papillary variety. According to authorities, papillary tumors constitute about three-fourths of renal pelvic growths. Of the 179 pelvic tumors re-

* Read before the Southern Surgical Association at Edgewater Park, Miss., December 15, 1936.

viewed by Smith, 142, or 79 per cent, were of the papillary type. Fifteen of Hunt's 23 cases were papillary and sessile. Five of my cases were papillary and two sessile.

The papillary tumors have a tendency to be multiple and occur more frequently in the male than in the female. In 1933, Joly, at the International Society of Urology, showed that of 208 papillary tumors of the renal pelvis, 177, or 73 per cent, occurred in the male. On the other hand, the squamous cell and other invasive tumors occur in about the same proportion in the male and female. Papillary tumors possess the notorious quality of involving other parts of the urinary system, particularly the ureter and the bladder on the corresponding side and occasionally the opposite ureter in 50 per cent of the cases either simultaneously or with recurrences; whereas the infiltrative squamous growths lack this trait. This decided difference has a definite bearing on the type of surgical procedure. Following the removal of a kidney for pelvic tumor, a gross pathologic inspection should be made, and in case the tumor is papillary, a nephro-ureterectomy with partial resection of the bladder is necessary, otherwise a nephrectomy will suffice. This peculiar characteristic on the part of papillary tumors to implicate other parts of the urinary tract is entirely different from any other type of renal neoplasm, but corresponds exactly to tumors of the same nature occurring in the bladder.

The various explanations of the associated involvement of the ureter have been the source of considerable controversy. Most of the articles on this subject bear such titles as "Tumors of the Renal Pelvis with Transplantation to the Ureter" or "Implantation to the Ureter," and so on. It is generally recognized that papillary tumors of the urinary tract have a decided tendency to occur in different portions simultaneously and to implant themselves on raw surfaces, the growth being active if such a surface is exposed to them. But with an intact ureter, it does not seem likely that the peculiar process can be called a veritable transplantation. It is a well known fact highly appreciated by those who have engaged in cancer research, that tumor cells do not implant themselves on an intact epithelial surface. It seems more likely that these tumors as well as similar tumors in the bladder result from a multiplicity as regards origin. I fully agree with Ewing and Keyes that there is every reason to believe that the multiplicity of these tumors is due to a cancerigenic irritation and not to direct implantation. Nevertheless one cannot shun the fact that with the same type of epithelium in the ureter as in the kidney pelvis, primary tumors of the ureter are exceedingly rare. Collected series have been reported by Kretschmer, Day, Mellicow and Findlay, Colston and Judd. For instance, at the Mayo Clinic, until 1921, only one case of carcinoma of the ureter had been observed, but in 1933 Snyder and Wood were able to collect 69 cases from the literature and add one of their own. In 1934, Mellicow and Findlay reported one case of papilloma of the ureter, but were able to collect only 28 others. This shows a decided discrepancy between the comparative frequency of pelvic tumors with ureteral involvement and primary ureteral neoplasms.

Tumors of other types rarely attack this canal. Hunt and Schacht have

each reported an hypernephroma of the ureter; Patch a granuloma; and the author an hemangioma.

Papillary growths of the renal pelvis are slow in their progress and not nearly so malignant as the nonpapillary tumors. They are seldom associated with any preexisting pathologic factors such as stone, leukoplakia and the like, whereas the nonpapillary growths are decidedly malignant and occasionally associated with stone, infection and leukoplakia.

In Kretschmer's series of 43 cases, 25 per cent of the nonpapillary growths were associated with stone, whereas less than 7 per cent of the papillary growths reported by Smith and Gilbert showed associated stone. The infiltrative squamous cell tumors are highly malignant and the eight patients reported by Hunt and a similar series reported by Kretschmer, died.

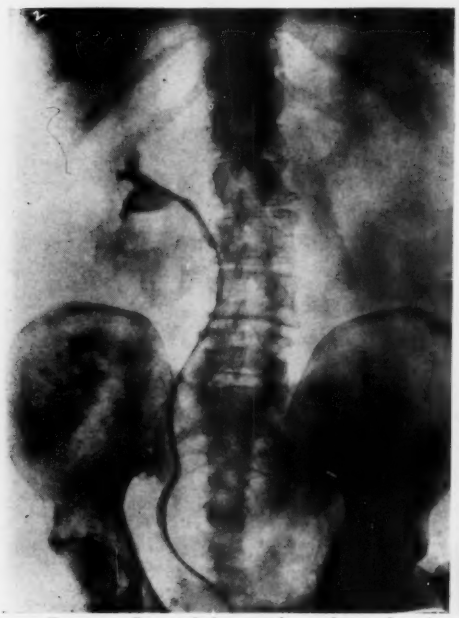


FIG. 1.—Case of hematuria and renal pain. Smooth symmetrical filling defect in kidney pelvis. Pyelographic fluid between it and pelvic outline. Amputation lower calyx. Large shadowless stone in renal pelvis simulating renal tumor.

FIG. 2.—Pyelogram showing filling defect of pelvic tumor. Other ureterograms showed no involvement of ureter. Nephro-ureterectomy February, 1936.

As a rule the associated tumors are similar in their histologic structure to the pelvic neoplasm. This has been true in two of my cases in which there were ureteral growths and yet the recurrences in the cases analyzed by Kimball and Ferris were sometimes dissimilar. For instance, in 26 cases of benign tumor of the renal pelvis in which there were recurrences, six of these recurrences were pathologically malignant. On the other hand, in 24 papillary carcinomata five of the recurrences were benign papillomata.

The diagnosis of pelvic tumors is made chiefly by urographic study. The majority are associated with profuse hematuria; rarely is there a palpable renal tumor except in instances of hydro- or hematonephrosis. Hence hematuria without definite palpable evidences of renal tumor may be deceptive.

Renal pain has been common in all of the cases reported and usually results from pelvic block with its resulting pyelectasis. Urographic evidences of filling defects in the pelvis and ureter may again be deceptive and may not represent neoplasm. They may occur as a result of a clot resulting from some other renal lesion, a shadowless stone, tuberculosis, cortical tumors of small size which may implicate the pelvis, occasionally indentures from spasm, granulomatous and cystic changes along the ureter and renal pelvis.

The diagnosis can be made only by thoroughly balancing accounts, paying strict attention to other phases of the clinical history and physical findings, rechecking repeatedly in case of doubt and never exploring except as a very last resort. If the filling defect is persistent upon repeated observations

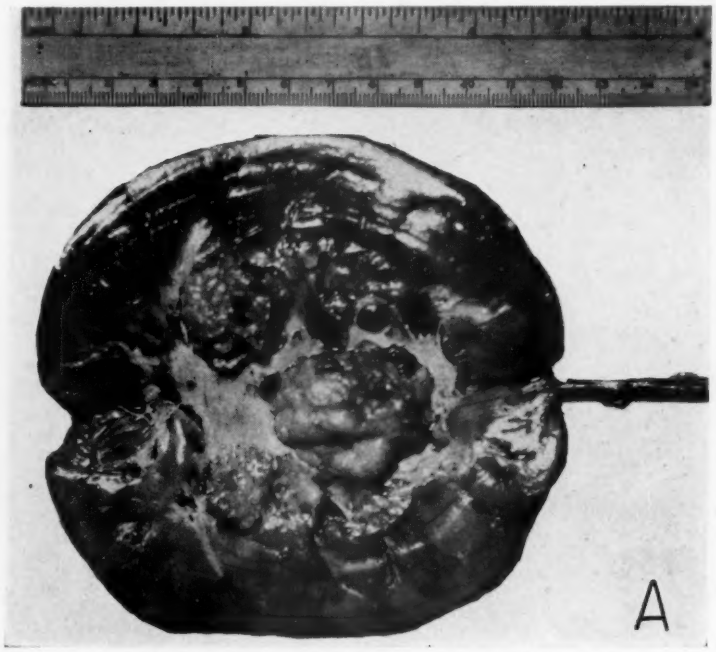


FIG. 2A.—Kidney showing multiple tumors, papillary carcinoma. Lower ureter not shown it having been completely sectioned for tumor, none demonstrated. Patient well 10½ months. No recurrence.

and there are no evidences of chronic infection or stone, and the observation is made at an interval between bleedings, the evidence is conclusive that such an abnormality is created by a pelvic tumor. Ureteritis cystica will occasionally present radiologic exhibits which may be very difficult to differentiate. Such lesions are more definitely confined to the ureter than to the pelvis of the kidney. There is usually evidence of infection and the lesion is more likely to be bilateral. It is seldom associated with hematuria. A recent case (Fig. 1) of a large shadowless stone in the pelvis, preventing filling of the lower calix, associated with hematuria, with negative roentgenogram on repeated examination, remained puzzling for some time, and it was only the smooth symmetrical outline of the filling defect and the fact

that there was the pyelographic material between the filling defect and the pelvis wall and an indefinite shadow on one film that made the diagnosis

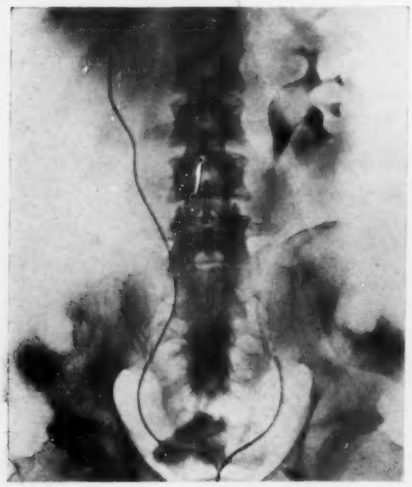


FIG. 3.—Pyelogram showing filling defect from papilloma of kidney pelvis. No demonstrable involvement of ureter at the time.

(B)—Recurrent hematuria. Papilloma projecting from ureteral orifice coagulated. Ureterogram one year and six months later. Note defects in the lower ureter. Ureterectomy.

possible. The filling defect occasioned by a tumor is usually irregular in outline and extends to the margin of the pelvis (Figs. 2 and 3).

Ureteral involvement is variable, seldom continuous, is more likely to

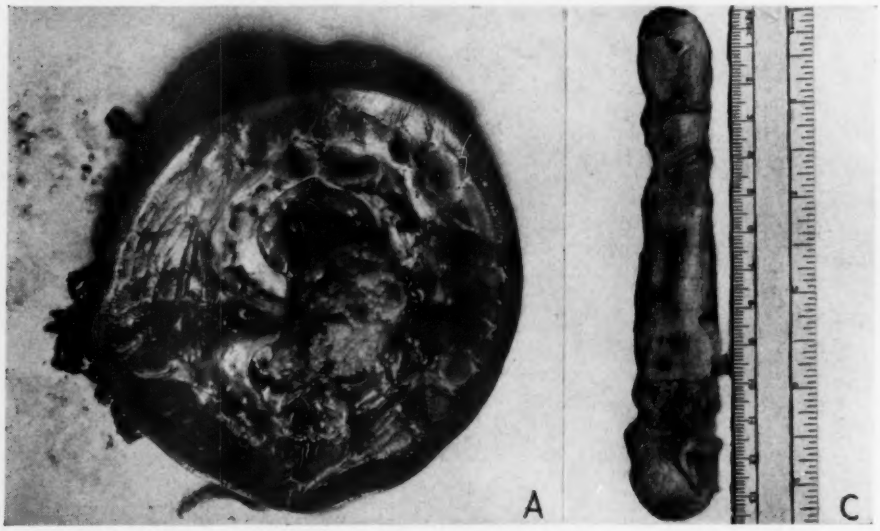


FIG. 3A.—Kidney specimen showing large papilloma of the pelvis.

(C)—Specimen of ureter showing multiple tumors at lower end. Few in the upper end. Patient living and well, no recurrence one year after ureterectomy.

occur in the region of the normal physiologic constrictions, particularly at the lower end of the ureter and in the region of the renal pelvis.

Occasionally it is impossible to diagnose these tumors, as in the case reported by James C. Anderson in which profuse hemorrhage from the kidney was the result of a very small papilloma, no larger than a grain of wheat, in one of the calices. Other instances of diagnostic difficulty occur when, due to occlusion of the pelvis by tumor or the tumor blocking the lower end of the ureter, it is impossible to inject the medium into the renal pelvis. Any tumor in the immediate neighborhood of the ureteral orifice should arouse one's suspicions of the presence of renal pelvic neoplasm (Fig. 4).

One of my cases (Fig. 5) revealed the occasional difficulty in arriving at

FIG. 4.—Large hydronephrotic kidney, interior of which was studded with a generalized papillary carcinomatosis. Kidney removed. Associated with carcinoma of bladder at ureteral orifice involving intramural ureter. Treated by cystoscopic applications and roentgen therapy. Bone metastasis. Patient died 4 months later.

an accurate diagnosis. A large palpable renal tumor, accompanied by hematuria, also showed a tumor mass projecting from the corresponding ureteral orifice with resultant filling defect of the ureter. The kidney was removed and the mass found to be due to a large hydronephrotic sac but contained no tumor growth. The hydronephrosis had resulted from obstruction due either to a primary tumor of the bladder with extension to the ureter or the reverse. The patient was an elderly woman and her condition did not warrant ureterectomy at the time. Several months later

she entered the hospital for the secondary operation but died of apoplexy before operation was attempted.

In two of the tumors of the series which is being presented, it was impossible to diagnose a pelvic tumor from the cystoscopic findings. Pyelograms were typical of renal neoplasm, and at operation it was found that the infiltrative squamous cell tumors had extended from the pelvis into the kidney substance and involved a large part of the kidney (Figs. 6 and 7).

Intravenous urography may be of assistance to the diagnostician in certain cases, but the delineation through this means is seldom as clean cut as through retrograde pyelography. In two of the cases in our series in which

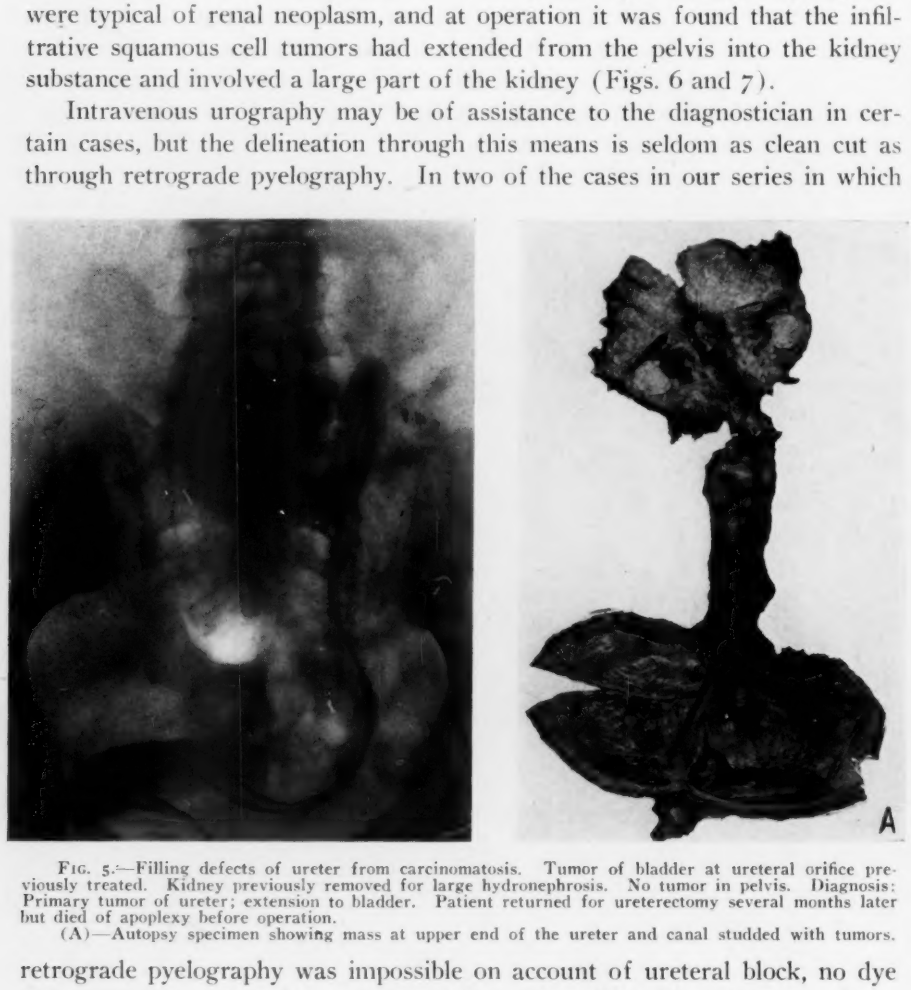


FIG. 5.—Filling defects of ureter from carcinomatosis. Tumor of bladder at ureteral orifice previously treated. Kidney previously removed for large hydronephrosis. No tumor in pelvis. Diagnosis: Primary tumor of ureter; extension to bladder. Patient returned for ureterectomy several months later but died of apoplexy before operation.
(A)—Autopsy specimen showing mass at upper end of the ureter and canal studded with tumors.

retrograde pyelography was impossible on account of ureteral block, no dye was excreted to give the necessary information (Fig. 8). Because of the necessity for absolute clarity of pelvic topography, retrograde pyelography is far superior to intravenous in the differential study of such neoplasms.

There is one clinical finding of importance in the diagnosis of pelvic neoplasm. The microscopic examination of bits of tissue in the urine or the examination of the washings from the renal pelvis with a recovery of tumor cells will prove of great assistance.

The treatment of tumors of the renal pelvis is surgical and varies with the type of the tumor. As in the case of all tumors, early diagnosis is most essential for the future welfare of the patient. Unfortunately, on account of

Volume 106
Number 1

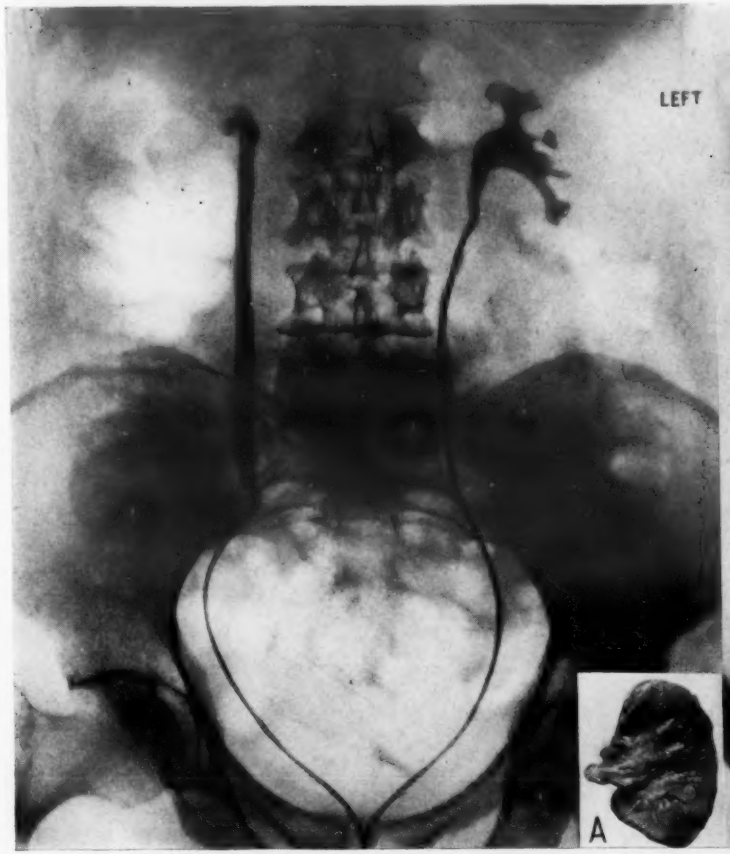


FIG. 6—Pyelogram showing practically no filling of pelvis except near ureteropelvic junction. Ureter demonstrates no filling defects. No palpable renal tumor. Diagnosis: Renal tumor. Right nephrectomy September, 1935. Living and well 14 months after nephrectomy. Diagnosis: Carcinoma of kidney pelvis with extension into renal substance. (A)—Kidney specimen showing marked invasion of pelvis and kidney.

FIG. 7.—Pyelogram left kidney. Diagnosis: Renal tumor. Large palpable tumor mass left kidney region. No hematuria. Metastasis to ribs and vertebrae. Preoperative roentgen therapy. Nephrectomy. Diagnosis: Squamous cell tumor of renal pelvis with marked extension into kidney substance. Regional lymph nodes found involved at operation. Patient died 4½ months later. (A)—Kidney showing extension of tumor into its substance.

hematuria being painless, these patients are not seen in the early stages of the disease, and in the squamous cell invasive tumors, the majority of the growths have extended beyond the hope of cure. The regional lymph nodes are often involved, hence the prognosis is poor. Simple nephrectomy is usually all that is necessary since these tumors possess little tendency to involve the ureter.

In spite of the fact that many of these pelvic tumors are not radiosensitive, it is always the part of prudence to subject such cases to preliminary roentgen therapy, particularly in the light of the recent reports of Keyes and Ferguson on the beneficial effects of such radiation on the papillary neoplasms of the bladder.

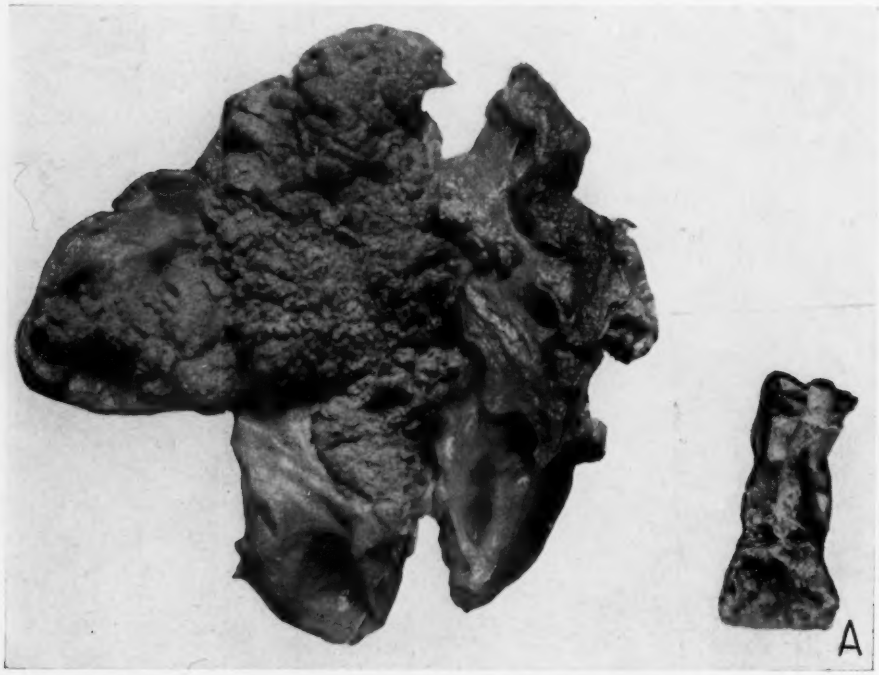


FIG. 8.—Large hydronephrosis. Kidney a mere shell, studded with papillary carcinoma. Removed January, 1933. Recurrence of hematuria three years, eight months later. Papillary tumor then projecting from ureteral orifice. Ureterectomy. (A)—Ureter shows multiple lesions of papillary carcinoma. Specimen shows lower end of ureter, remaining ureter no tumor, serially sectioned and not shown. Patient now well, almost four years after nephrectomy and four months after ureterectomy.

In the group of papillary tumors, benign and malignant, more than nephrectomy is required, although this is the operation which has been performed as the initial one in the majority of instances.

I shall quote from the article by Kimball and Ferris reporting 74 cases of such tumors which involved more than one portion of the urinary tract. "Forty were treated by nephrectomy and 25 by nephro-ureterectomy not including the intramural part of the ureter. Of the 40 cases treated by nephrectomy 30, or 75 per cent, had recurrences, 21 of these required a secondary ureterectomy with further recurrence in 12 or 57 per cent. The known mortality in this group treated by nephrectomy was 33 per cent.

Primary nephro-ureterectomy was performed without including the intramural part of the ureter in 25 cases; there were known recurrences in 17 or 68 per cent. A further resection of the intramural portion of the ureter was effected in 12 instances with further recurrences in four cases. The known mortality for this group was 44 per cent.

"Only six cases were treated by primary nephro-ureterectomy which included the intramural part of the ureter. In these cases there were two diagnosed as benign and four as malignant. The known mortality in the malignant

FIG. 9.—Ureterogram showing filling defect of the ureter. Hematuria. Kidney removed elsewhere 18 months previously. Large mass involving upper ureter and surrounding structures. Specimen shows carcinoma. Ureterectomy. Died one year, three months after ureterectomy and radium implantation, three years after nephrectomy.

group was 25 per cent. In the benign group both cases were living at the end of 11 years.

"Of the total 74 cases, there were 28 known deaths, a mortality of 38 per cent. When we consider that 33 per cent of this group, 74 collected cases, had tumors in the ureter and bladder, as well as in the kidney, at the time they consulted an urologist, and when we consider that 86 per cent of all the recurrences appear in the remaining ureteral stump and ureteral

orifices, we must, therefore, choose a method of treatment which will remove the disease in its entirety."

From a survey of the cases which have been reported and from personal experience, it is evident that all papillary tumors of the renal pelvis, whether associated with ureteral or vesical involvement or not, should require a complete nephro-ureterectomy with removal of the intramural ureter or destruction of it. This should preferably be accomplished in one operation or as soon as possible after the original nephrectomy. The complete operation is not a difficult one if primarily performed.

If the ureter is removed secondarily, the operation may offer considerable difficulty, particularly if the tumor involves the upper part of the ureter and is associated with peri-ureteritis. In one of the cases reported in this series (Fig. 9) there was a tremendous tumor mass involving the upper end of the ureter which was adherent to the surrounding structures in the neighborhood of the deep vessels, and made the dissection extremely difficult. Tumor involvement at the lower end of the ureter with surrounding reaction, while not as dangerous in removal, is often difficult to extirpate in its entirety, and the prognosis is less favorable.

Several technics have been proposed, the most favored one at present, and the one which to me is unquestionably the most satisfactory, is a combined lumbar and lower midline exposure. The first nephro-ureterectomy, as far as I can determine, was performed by Howard Kelly in 1893. Henry Morris in his "Surgical Diseases of the Kidney and Ureter" gives Poncet (1891) the credit, but it appears that this author did not remove the vesical portion. Kelly's first case was operated upon in two stages; his second, several years later, was performed by the combined retroperitoneal and vaginal technic in one sitting. In 1901, Kelly again performed this operation, utilizing the retroperitoneal and transperitoneal routes. In 1914, Lower performed an extraperitoneal nephro-ureterectomy in two stages with a three months interval, the latter through the lower iliac incision. Bissell, in 1903, suggested the complete transperitoneal extirpation of the kidney, ureter and part of the bladder wall, and again, in 1908 and 1915, urged the advantages of this exposure over other technics for stone and tuberculosis. In 1925, he suggested this intra-abdominal technic for papilloma of the renal pelvis with ureteral implants, claiming that in the female the broad ligament and the uterine vessels and nerves made the extraperitoneal operation difficult and unsafe. This type of operation today has few, if any, supporters. The extraperitoneal procedure in both the male and female is the method of choice. The combined lumbar and suprapubic exposures afford the best access to the different parts of the operative field, making the technical procedures much simpler and assuring a safer and sounder healing of the abdominal wall.

During the process of the lumbar nephrectomy the ureter is freed as far down as is convenient, usually over the pelvic brim. It is then doubly clamped. After thorough walling off, both ends should be carefully ligated, in case the clamp should slip, in order to prevent any possibility of soiling.

The lower segment of the ureter should be reinforced by stout material, preferably tape, which is to be utilized later for the purpose of traction. The ureter is divided by cautery between the clamps and the kidney removed. The incision is closed except for drainage and the ligature on the lower end of the ureter brought out of the wound. The patient is then put in a moderate Trendelenburg position and a midline incision is made above the pubis. The bladder, which has been previously emptied, is freed on the side on which the ureter is to be removed and thoroughly mobilized. With an assistant making traction on the tape, the ureter is made taut and is readily palpable through the lower wound, and is pulled through from above. It is then grasped and stripped to the bladder. Then by firm traction on the ureter the bladder base is elevated and the ureteral insertion brought easily into view. The utilization of the ureter as a tractor is the greatest adjunct in the removal of its vesical insertion. The area of the bladder wall con-

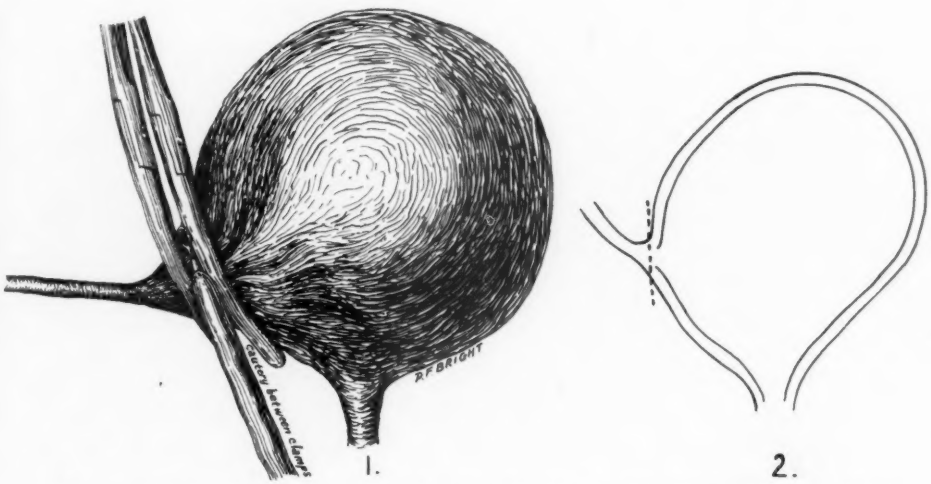


FIG. 10.—(1) Traction of ureter upwardly—funneling bladder with intramural ureter. Clamps applied containing intramural ureter and bladder wall. Closed resection with cutting current insuring against implantation. (2) Slight funneling of bladder from gentle traction of ureter. Dotted line shows site of ligation including part of bladder wall and intramural ureter, preventing ureteral mucous membrane from remaining external to bladder wall. Remaining intramural ureteral mucosa later destroyed by coagulating current through cystoscope.

taining the intramural ureter is funneled outwardly (Fig. 10 [1 and 2]). It is doubly clamped and resected between clamps with a cautery or cutting current and is sutured with the lower clamp *in situ*. This prevents exposure and contamination of the operative field, and safeguards against implantation, the most essential feature of the whole operative procedure. This funnel operation is much simpler, shorter, and safer than other open dissection methods.

In case complete mobilization is not possible, and this closed method is not permissible in its entirety, ureteral traction will still be of worth and value. The bladder area is made taut and can then be easily resected by a circular incision with the cutting current. This procedure is consummated

without delay after which the ureter with the vesical cuff is immediately pulled out of the wound with a minimum chance of soiling.

In case there is a tumor in the lower ureter projecting into the bladder, it should be previously destroyed by coagulation through the cystoscope before the open operation is attempted. In other words, every possible method of preventing cellular implantation should be observed. The open operation described by Hunt exposes the tumor to a raw surface and predisposes to implantation which should be avoided, if possible, and it is my opinion that the operation which I have described succeeds in this respect.

In certain cases in which there is no demonstrable evidence of tumor formation in the ureter, a partial resection of the intramural ureter may be effected. In this type of operation the bladder is not funneled out as much as in the previous one, but enough to assure the operator that the entire ureter external to the bladder is being removed. With this slight funneling of the bladder wall the ligature is applied, containing both the external coat of the bladder and ureter. In this way a small part of the intramural ureter is removed but the ureterovesical valve is preserved, and the chance of urinary regurgitation prevented. This eliminates the necessity for indwelling catheter drainage, and minimizes the chances of postoperative discomfort, fistula, and urinary infection. The remaining part of the intramural ureter must be thoroughly coagulated transurethrally within a week or ten days. This should guarantee freedom from recurrence. Colston, in 1933, in removing a ureter for a primary ureteral tumor, destroyed the intramural ureter during the operation by means of electrocoagulation applied through the ureteral stump. Aseptic nephro-ureterectomy described by Beer and consisting in removing the kidney and ureter intact is an excellent operation, but is, as a rule, technically somewhat more difficult than with ureteral section, and seems to possess no particular advantage, if one is careful with the ureteral stumps. It possesses the disadvantage of not permitting a gross pathologic inspection of the tumor in the operating room, the true surgical guide as to the indication for ureterectomy. The utilization of the proximal ureter as a tractor facilitates nephrectomy as strikingly as the use of the lower ureter simplifies partial cystectomy.

It seems heroic to remove the kidney and ureter for a small papilloma in the pelvis when these tumors are so easily destroyed by electrocoagulation. I have felt tempted to do it but even with the exercise of every protective precaution, opening the pelvis would be almost certain to invite implantation.

Primary ureteral tumors usually require the same surgical procedure. As far as I have been able to determine, there have been but two tumors which have been removed from the ureter without renal sacrifice, and these are: The case of granuloma reported by Patch, in which the tumor was removed by resection of about an inch of the ureter with reanastomosis, and the author's case of hemangioma of the lower end of the ureter which was easily dissected from around the ureter leaving the canal intact.

SUMMARY OF SEVEN CASES OF TUMORS OF THE RENAL PELVIS OCCURRING ON THE UROLOGIC SERVICE OF THE BARNES HOSPITAL

Age—average 53. 1 35 years
3 40 to 49
1 50 to 59
1 60 to 69
1 70

Sex—5 males, 2 females

Race—5 white, 2 colored

Symptoms:

Initial

2—Hematuria

4—Renal pain

1—Twitching sensation in right thigh with loss of weight and mass in renal region.

Hematuria present in 6 cases

Renal pain present in 5 cases

Duration of Symptoms: Average 13½ months

Longest 2 years

Shortest 1 month

Associated Conditions:

Bladder tumor in 1 case, and appeared later in another as a recurrence following nephrectomy. Both of these were papillary tumors.

Infection present in 2 cases.

No stones in any case.

Palpable mass in 3 cases, one due to large hydronephrosis with papillary carcinoma; a second from recurrence of a mass in the stump of the ureter following nephrectomy for tumor; and a third a squamous cell carcinoma arising in the pelvis, and involving the kidney substance.

Metastases were present in 2 cases, both to the lumbar vertebrae and one of these questionably also to the ribs.

Ureteral involvement occurred in 3 cases, necessitating secondary ureterectomy. Two of these were of the papillary type and the third was a recurrence of a large mass around the stump of the ureter following nephrectomy for renal tumor of unknown type (nephrectomy performed elsewhere).

Roentgen Therapy: Preoperative in 3 cases. Postoperative in two others and one implantation of radium at the time of operation, which was removal of stump of ureter with the mass at the upper end.

Diagnosis: Urograms were made in 5 cases. In the other two the ureter could not be catheterized.

A diagnosis of renal tumor was made in 3 cases and of recurrent carcinoma of the ureter secondary to kidney tumor in one.

A diagnosis of pelvic tumor was made in 3 cases.

Operation: Nephrectomy alone was performed in 6 cases, one of these elsewhere and the seventh case had complete nephro-ureterectomy.

Three cases had later ureterectomies for recurrence.

Surgical Pathology:

Papillary carcinoma of renal pelvis	3 cases
Papilloma of renal pelvis	1 case
Squamous cell carcinoma of renal pelvis	2 cases
Nephrectomy performed elsewhere; type of tumor not known.	1 case

Follow-Up:

Four living and well with no recurrence (3 papillary type, 1 squamous).

Three dead (1 of squamous type, 1 papillary, 1 unknown pathology).

Of the three dead—One lived 4½ months after nephrectomy for squamous cell carcinoma or one year after onset of symptoms.

One lived 1 yr., 3 mos. after ureterectomy for recurrence, 3 yrs. after nephrectomy for renal tumor or 3 yrs., 8 mos. after onset of first symptoms. The other, a papillary carcinoma with bone metastasis, lived 4 mos. after operation, and 5 mos. after onset of symptoms.

Of those living (4)

One living 4 mos. after secondary ureterectomy, 4 yrs. after nephrectomy for papillary carcinoma of pelvis or 5 yrs., 2 mos. after onset of initial symptom of hematuria.

One living 11 mos. after secondary ureterectomy, 2 yrs., 4 mos. after nephrectomy for papilloma of pelvis or 4 yrs., 6 mos. after onset of symptom.

One living 14 mos. after nephrectomy for squamous cell carcinoma of pelvis or 3 yrs., 2 mos. after onset of first symptom.

One living 10½ mos. after nephro-ureterectomy for papillary carcinoma of pelvis or 2 yrs., 3 mos. after onset of first symptom.

Duration of Life:

Of the 3 dead—Average 21 mos. after onset of symptoms.
Average 16 mos. after nephrectomy.

Of the 4 living—(1 squamous cell carcinoma, 2 papillary carcinoma and 1 papilloma)

Average 45 mos. after onset of symptoms.
Average 25 mos. after nephrectomy, nephrectomy with secondary ureterectomy or nephro-ureterectomy.

CONCLUSIONS

(1) Primary tumors of the renal pelvis are rare.

(2) They are, as a rule, papillary in structure.

(3) They possess a striking tendency to invade other portions of the urinary system, especially the corresponding ureter. Such involvement occurred in three of the five cases (60 per cent) of papillary tumors in this series.

(4) This inherent characteristic makes it necessary to perform complete nephro-ureterectomy with removal or destruction of the intramural ureter.

(5) The operation described, of closed resection of the bladder wall containing the intramural ureter—the funnel operation—seems to possess decided advantages over the open ones in protecting against implantation recurrence.

(6) Utilization of the ureter as a tractor greatly simplifies the technic.

REFERENCES

The reader is referred to article by Smith and Gilbert[34] having a bibliography of 151 articles, for references prior to 1925.

[1] Anderson, J. C.: Persistent Hematuria, from Minute Papilloma of Renal Pelvis. Brit. Jour. Surg., **17,** 696–698, April, 1930.

[2] Bissell, D.: Renal Papillomata and Ureteral Implants, Their Surgical Treatment in the Female; with Report of Case. Surg., Gynec., and Obstet., **40,** 323–333, March, 1925.

[3] Body, M. S.: Infected Supernumerary Ureter and Pelvis of Kidney with Heminephrectomy. ANNALS OF SURGERY, **98,** 119–124, July, 1933.

[4] Bothe, A. E.: Papilloma of the Renal Pelvis. Jour. Urol., **22,** 46–54, July, 1929.

[5] Cattaneo, L.: Cyst in Congenital Ectopic Pelvis Simulating Adnexal Tumor. Folia gynaec., **24,** 455–490, 1927.

[6] Caulk, John R.: Hemangiomata of the Bladder and Ureter. Surg., Gynec., and Obstet., p. 49, July, 1925.

[7] Colston, J. A. C.: Primary Tumors of the Ureter: A New Method of Complete Nephro-ureterectomy. Bull. Johns Hopkins Hosp., **55,** 6, 361.

[8] Compani, V.: Tumors of Ureter and Pelvis; Diagnosis and Treatment. Ann. d. Hosp. de Santa Crew i Sant Pau., **8,** 5–7, January 15, 1934.

[9] Day, R. V., Fairchild, F. D., and Martin, H. W.: Plan for Early Diagnosis and Management of Primary Papilloma of Ureter and Kidney Pelvis Tumors, Case Report of Each. Surg., Gynec., and Obstet., **40,** 485–492, April, 1925.

[10] Dozsa, E.: Villous Tumors of Renal Pelvis and Ureters. Ztschr. f. urol. chir., **22,** 81–103, 1927.

[11] Gorash, V. A.: Tumors of Renal Pelvis. Vestnik khir. (Nos. 58–60), **20,** 344–354, 1930.

[12] Henline, R. B.: Cause and Treatment of Noncalculous Ureteropelvic Obstructions, with Report of 66 Operated Cases. Jour. Urol., **34,** 584–614, December, 1935.

[13] Hunt, V. C.: Hypernephroma Progressing along Ureter. Surg. Clin. N. Amer., **7,** 1460–1462, December, 1927.

[14] Hunt, V. C.: Papillary Epithelioma of Renal Pelvis. Jour. Urol., **18,** 225–246, September, 1927.

[15] Iwamoto, M.: Partial Pyonephrosis with Calculi in Case of Double Renal Pelvis and Double Ureters. Mitt. u. allg. Path. u. path. Anat., **4,** 283–296, April 26, 1928.

[16] Judd, E. S.: Papilloma of the Renal Pelvis. Surg. Clin. N. Amer., **9,** 11–12, February, 1929.

[17] Judd, E. S., Parker, B. R., and Morse, H. D.: Tumors of the Kidney and Ureter and Tuberculosis of Kidney. Surg. Clin. N. Amer., **6,** 1137–1152, October, 1926.

[18] Kimball, F. N., and Ferris, H. W.: Papillomatous Tumor of Pelvis Associated with Similar Tumors of Ureter and Bladder; Review of Literature and Report of Two Cases. Jour. Urol., **31,** 257–304, March, 1934.

[19] Kimball, F. N.: Benign Papilloma of Pelvis. Am. Jour. Surg., **10,** 576–577, December, 1930.

[20] Kümmell, H.: Tumors of the Renal Pelvis and Ureters. Monatschr. f. Harkrank. u. sex. Hyg., **2,** 195–213, October 1, 1928.

[21] Laqueur, B.: Polypous Fibroids in Kidney Pelvis. Ztschr. f. Urolog. Chir., **17,** 205–212, 1925.

[22] Laurent, G., and Delvigne, M.: Retrograde Pyelography by Injection with Thorotrast (Thorium Dioxide Preparation) in Diagnosis of Papillomatous Tumor of Pelvis and Ureter. Ann. Soc. méd.-chir. de Liége, No. 2, 194–198, 1933.

[23] Laurent, G., and Delvigne, M.: Retrograde Pyelography with Injection of Thorotrast (Thorium Dioxide Preparation) in Diagnosis of Papillomatous Tumor of Pelvis and Ureter. Liége méd., **27,** 129–136, January 28, 1934.

[24] Lazarus, J. A.: Localization Pedunculated Hypernephroma Associated with Renal Ureteral Calculi. Urol. and Cutan. Rev., **39,** 551–553, August, 1935.

[25] McKenzie, D. W., and Ratner, M.: Tumors of the Renal Pelvis; Review of Literature and Report of a Case. Jour. Urol., **28,** 405–418, October, 1932.

[26] Negro, M.: Pathology of Papillary Tumors of Renal Pelvis; Cases. Arch. ital. di urol., **6,** 269–302, June, 1930.

[27] O'Farrell, T. T.: Malignant Papilloma of Renal Pelvis; Case. Irish J. Med. Sci., pp. 81–82, February, 1928.

[28] Olper, L.: Bilateral Adenomatous Polyposis of Ureters and Pelvis; Case. Arch. ital. di urol., **12,** 557–567, May, 1935.

[29] Pascual, S., *et al.*: Tumors of Pelvis and Ureter. Brit. Jour. Urol., **5,** 323–339, December, 1933.

[30] Patch, Frank S., and Rhea, L. J.: On the Pathogenesis of Bleeding in Tumors of the Kidney. Trans. Am. Assn. G. U. Surg., **23,** 123, 1930.

[31] Ralphs, F. G.: Sarcoma of the Renal Pelvis, Associated with Hydronephrosis. Brit. Jour. Surg., **13,** 190–192, July, 1925.

[32] Schacht, F. W.: Hypernephroma; Extension of Ureter. Surg., Gynec., and Obstet., **53,** 102–104, July, 1931.

[33] Simpson, C. M.: Malignant Tumors of the Pelvis. Texas State Jour. Med., **26,** 787–791, March, 1931.

[34] Smith, G. G., and Gilbert, A. C.: Malignant Papilloma of Kidney Pelvis. Jour. Urol., **13,** 25–42, January, 1925.

[35] Swartz, E. O.: Malignant Papilloma of Renal Pelvis Associated with Solitary Cyst of Kidney. Jour. Urol., **13,** 295–307, March, 1925.

[36] Thomson-Walker, J.: Ureterectomy for Papilloma; 3 Cases with Comments. Brit. Jour. Urol., **1,** 141–149, June, 1929.

[37] Walters, W., and Braasch, W. F.: Nephrectomy and Nephro-ureterectomy for Malignant Tumors. Am. Jour. Surg., **28,** 23–31, April, 1935.

[38] White, E. W., and Ritch, C. O.: Primary Papillary Epithelioma of Renal Pelvis, with Report of Case. Jour. Urol., **15,** 143–153, February, 1926.

PHEOCHROMOCYTOMA WITH DEMONSTRATION OF PRESSOR (ADRENALIN) SUBSTANCE IN THE BLOOD PREOPERATIVELY DURING HYPERTENSIVE CRISES

EDWIN BEER M.D., F. H. KING, M.D., AND M. PRINZMETAL M.D.
NEW YORK, N. Y.

FROM THE SERVICES OF THE MOUNT SINAI HOSPITAL, NEW YORK, N. Y.

THE following case report is placed on record to call attention to this clinical entity and to report some interesting observations made during the stay of the patient in the wards of the hospital and during the follow up after her discharge. Though Kohn described the chromaffin system in the abdomen about 40 years ago, judging from the literature, interest in neoplastic changes in this system has stirred the profession only recently. Case reports[1] of tumors derived from this system, both in the medulla of the adrenal and in the adjacent sympathetic nerves, though still exceedingly rare, are becoming more frequent during recent years, and every new case that is published is helpful to better understanding and earlier recognition of these curious growths, called paragangliomata or pheochromocytomata. To date only six cases of pheochromocytomata in the adrenal gland have been recorded, after successful removal of the growth. In addition, two cases have been reported in which the growths were outside the adrenal gland in the local sympathetic distribution (Mayo-Leriche Bauer). The case here recorded involved the left adrenal gland and operative removal of the large pheochromocytoma seems to have produced a complete relief.

Case Report.—A white female, single, age 26, was admitted to the Mount Sinai Hospital with the history of having nine years previously first noted the insidious onset of infrequent sensations of mild fatigue, throbbing headache and sweating at intervals. These symptoms were attributed to hyperthyroidism and she was subjected to subtotal thyroidectomy, without subsequent relief. Microscopic examination of the removed thyroid tissue proved it to be an adenocarcinoma. Sections obtained by request were examined by the pathologist at this hospital, who concurred in the diagnosis.

Her symptoms gradually increased in severity and about seven years ago she noted that the distal phalanx of the right index finger would, on occasion, suddenly become perfectly white, changing to a purple color which in turn would become replaced by an angry red. During the two years prior to admission, this phenomenon had extended to involve all the digits of both hands, and to a lesser extent the toes. For three years she had noted that the distal portion of the upper and lower extremities, as well as the tip of the nose, constantly felt cold, regardless of the season. Other cutaneous changes noted were a reddish-cyanotic discoloration of the skin around the ankles and a reddish-purple mottling and reticulation of the skin of the upper and lower extremities, most marked about the knee joint.

The patient complained chiefly of attacks in which the symptoms presented themselves in a fairly definite sequence. These episodes began with nausea and an intense, generalized headache. Her hair felt as though it were standing on end and being

Submitted for publication February 20, 1937.

pulled. This was soon followed by definite precordial throbbing with a subjective feeling of markedly exaggerated pulsations of the vessels of the neck. She was dyspneic and on occasions found herself gasping for breath. Her fingers then underwent the series of color changes already described. These symptoms soon abated, leaving her drenched with perspiration and utterly fatigued. Such attacks lasted about five minutes. Until about three months before entering the hospital, these episodes would occur once a week. After that they gradually increased in frequency and severity so that just before hospitalization, they were occurring almost every half hour. She had been informed by her physician two months previously that her blood pressure was 190-200. During the past four years, there had been a gradual loss in weight of 18 pounds, notwithstanding an excellent appetite.

The family history was of unusual interest. Both her mother and sister had had thyroidectomies; moreover, an older sister who had also had a thyroidectomy died at the age of 28, with a clinical picture strikingly suggestive of that presented by the patient herself, and which was believed to have been (according to the hospital record) a rare disturbance of the sympathetic system.

Physical Examination.—The patient was a thin, underdeveloped, young, white female, who appeared chronically ill and sweated profusely. The fundi showed a very slight thinning of the arteries with increased light reflex. There was a well healed collar incision at the base of the neck. The lungs were normal. The heart was not enlarged and its sounds were of good quality. The aortic second sound was louder than the pulmonic. A rough systolic murmur was present at the base. The radial vessels seemed, on palpation, to be moderately sclerotic. The blood pressure at the initial examination was 230/180. A slight fine tremor of the outstretched fingers was present. Abdominal examination was negative.

She continued to have attacks as previously described, in the hospital. At such times her blood pressure rose from 140/100 to 280/200. On the basis of this clinical picture, a presumptive diagnosis of an adrenal paraganglioma was made.

Laboratory Data.—The blood count was normal. Urine examination showed a normal concentration. Chemical examination of the blood showed the urea to be 25 mg., sugar 175 mg., cholesterol 425 mg., and sodium 138.3 milli-equivalents. The basal metabolic rate was, on three different occasions, plus 69, 39 and 27 per cent. The electrocardiogram showed a sinus tachycardia with a rate of 115 per minute, left ventricular preponderance, QRS of high voltage, slight depression of the R-T transition in leads 1 and 2, and upright T4. Oscillometric determinations showed diminished peripheral oscillations, there being only a flicker at the ankle level. There was a diminution of skin temperature of the peripheral portions of the body, as determined by dermotherm readings. The Janney test showed a fasting blood sugar of 65 mg. per 100 cc., with a rise to 240 mg. at the end of one hour, followed by a fall to 50 mg. at the end of three hours. The patient was given an insulin test, consisting of the injection of ten units of insulin while fasting, the fasting blood sugar being 105 mg. per 100 cc. One and one-half hours later, the patient went into profound hypoglycemic shock, the blood sugar at this time being 15 mg. per 100 cc. She, however, responded promptly to intravenously administered glucose. Epinephrine sensitivity was determined by the subcutaneous injection of two minims of adrenalin (1-1000), and there was an unusually high rise in the blood pressure, indicating an abnormal sensitivity. Investigation of the urine for hormones disclosed a slight amount of gonadotropic hormone but no estrin.

Demonstration of Pressor Substance in the Blood during Hypertensive Crises.—An investigation was undertaken to demonstrate the presence of a pressor substance in the blood. During an attack induced by exercise, at which time the systolic blood pressure was over 300, 200 cc. of blood were removed from the antecubital vein and its pressor effect compared with the blood of a control subject, by a modification of the Pissemski method of perfusion of the denervated rabbit's ear. This method had been found to be

sensitive to epinephrine in as high a dilution as 1 in 100,000,000. Not more than 35 minutes elapsed between the phlebotomy and the experiment.

A constant inflow pump was used. If the vessels constrict, the fluid in the manometric tube rises, and vice versa. The perfusion was started first with control plasma. After a base line was reached, the subject's plasma was substituted. A remarkable pressor effect resulted. This was repeated three times (Chart 1). The ear was then perfused with 1-300,000 solution of ergotamine tartrate. Following this procedure, it was again perfused with the two plasmas. The pressor effect had now disappeared (Chart 1). These observations demonstrated the presence of an active pressor substance in the circulating blood, which, in view of the reversal effect of ergotamine, is almost certainly adrenalin.

In view of the history and observations made on the Medical Service, it was evident that the patient was probably suffering from a pheochromocytoma of the adrenal medulla

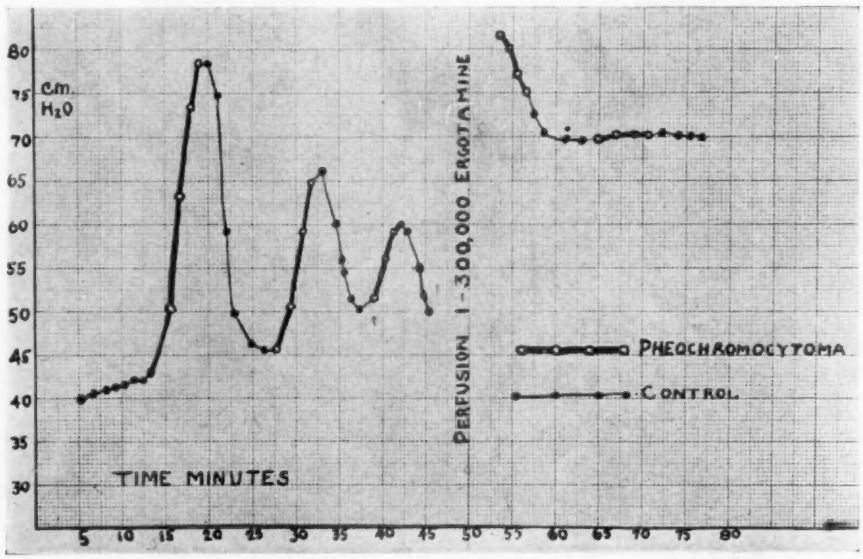


CHART 1.—Illustrating pressor effect of patient's plasma when perfused through denervated rabbit's ear and the reversal effect of ergotamine.

or adjacent sympathetic nerves. Before surgical removal could be attempted, however, it was necessary to determine which side was involved. One of the flat roentgenograms of the abdomen showed a diffuse but rather homogeneous shadow above the position of the left kidney; a retrograde pyelogram of this side showed that the left kidney had been pushed down, so that the pelvis was opposite the body of the third lumbar vertebra, and the upper calix showed definite pressure from above downward (Fig. 1). To outline the adrenal tumor, which was thought to be on the left side, a perirenal insufflation was undertaken by Doctor Mencher, which, in the anteroposterior and even better in the lateral view, outlined the left kidney and the large adrenal tumor situated directly above it, but separated from the kidney's deformed upper pole by a narrow linear gas band (Figs. 2 and 3). Studies of the right kidney showed it to be normal.

Operation.—May 29, 1935. Preoperative Diagnosis: Left adrenal pheochromocytoma. Anesthesia, avertin, supplemented by gas-oxygen. Intravenous glucose drip was begun before the operation. The kidney was readily located through a left lumbar incision. Above it, a very large, more or less spheroidal mass, occupying the region of the adrenal gland, was palpated and found displacing the kidney downward. The vascular pedicle of the kidney was seen to run into the capsule of the adrenal tumor, and a loop was

FIG. 1.—Retrograde pyelogram of the left kidney showing depressed kidney with compression of the calices in the upper pole.

FIG. 2.—Anteroposterior roentgenogram after perirenal insufflation, outlining clearly the large left adrenal tumor. Left kidney is surrounded with air and Gerota's fascia is filled with air.

FIG. 3.—Lateral oblique roentgenogram after perirenal insufflation, showing clearly the adrenal tumor, surrounded by the injected air, and below the adrenal tumor the much smaller kidney mass. Here again Gerota's space is full of injected air.

passed around the vessels, without tying them. Attempts to pull the renal pedicle toward the midline showed that it was impossible to separate the vascular structures from the adrenal tumor, and the ligature about the vessels was tied and the kidney removed, thus properly exposing the tumor, which ran up under the left leaf of the diaphragm. A number of vessels were tied during the delivery of the adrenal mass, which was about the size of a large grapefruit. The tumor was finally sufficiently liberated to afford access to its pedicle, which consisted of a very large vein, about one and one-half centimeters in diameter, which could be felt crossing the aorta, running into the vena cava.

Despite these manipulations, it was interesting to note that repeated blood pressures taken throughout the operation failed to show any rise, as one would have expected as the result of throwing adrenalin into the general circulation. During the operation at one time the systolic blood pressure dropped to 80. The operation was practically bloodless, and the wound was closed in layers in the usual way, with a small rubber drain. Following the operation, the patient was given a transfusion on the operating table.

The patient withstood the operation very well and, though somewhat shocked, made an uneventful recovery. The wound healed by primary union, except for slight retention.

Pathologic Report.—Macroscopic Examination: The specimen consisted of a globoid mass, weighing 290 Gm. and measuring 9 x 9 x 6 cm. (Fig. 4). The mass was well encapsulated. The capsule averaged 1 Mm. in thickness and its external aspect was rather smooth and even, except for scattered (1-3 cm. in diameter) projecting bosses. Along one edge of the specimen were a few fragments of yellowish brown tissue, which morphologically resembled adrenal cortex. In one portion immediately beneath the capsule was a nodule, the surface of which was dark brown-white. Its cortical rim was light yellow and bore a striking resemblance to minute adrenal glands. On section, the basic structures of adrenal gland, from which this mass presumably originated, were not distinguishable. Sectioned surface was fleshy in appearance and consistency. The surface, although rather smooth, consisted of irregularly sized lobules due to the presence of scattered smooth, delicate connective tissue strands. The surface further was irregularly mottled dull yellowish-pink, with innumerable flame-shaped rounded and less regular hemorrhagic zones (old and recent). In addition, there were several pea-sized and larger necrotic foci.

FIG. 4.—Gross appearance of cross-section of large adrenal tumor, which measures 9 x 9 x 6 cm. On the surface of the tumor are irregular projections made by the remains of adrenal cortex.

Microscopic Examination.—Sections stained with hematoxylin and eosin revealed the tumor to be composed of nests and anastomosing bands of round, spindle-shaped, and large polygonal cells, separated by very thin strands of connective tissue containing small blood vessels. Several areas of hemorrhage were noted, located mainly at the periphery. The cytoplasm of the tumor cells was granular and basophilic. The nuclei varied markedly in size and some of them appeared pyknotic. Sections of tissue fixed in Zenker's fluid showed a sparse distribution of brown colored pigment granules within the cytoplasm of the tumor cells, confirming the chromaffin nature of the growth. Between the cells and within the cytoplasm of some of them were noted ovoid bodies,

having a hyalin appearance and staining deeply with eosin. Stained with azocarmine, these bodies had a grayish-blue color and with phosphotungstic and hematoxylin they took a mahogany or light brown color. Only an occasional mitotic figure was noted. No ganglion cells were present. Sections stained for glycogen did not disclose this substance, nor was fat demonstrated after staining with sudan (Fig. 5). Sections of the removed kidney showed only mild arteriosclerosis. *Diagnosis:* Pheochromocytoma and kidney arteriosclerosis.

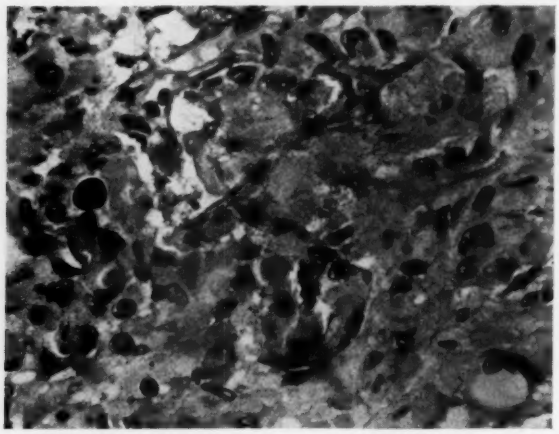


FIG. 5.—Histologic appearance of tumor (hematoxylin and eosin stain). Note deeply staining, hyalin-like body.

Further studies of the removed tumor were made by Doctor Frank, who was unable to demonstrate any gonadotropic hormone in the tumor tissue. A saline extract was made of the tumor tissue, which caused marked blanching when applied to a slightly scarified skin, showing that it contained an active constrictor element.

Postoperative Course.—The patient was considerably improved. There were no more systemic episodes and the blood pressure remained at 125/85. The previous cutis reticularis and discoloration of the skin above the ankles were no longer present. The tachycardia was much less marked. Her eye grounds still showed slight thinning of the vessels.

The laboratory procedures, done preoperatively, were repeated following the patient's return to the Medical Service, and the data obtained were as follows:

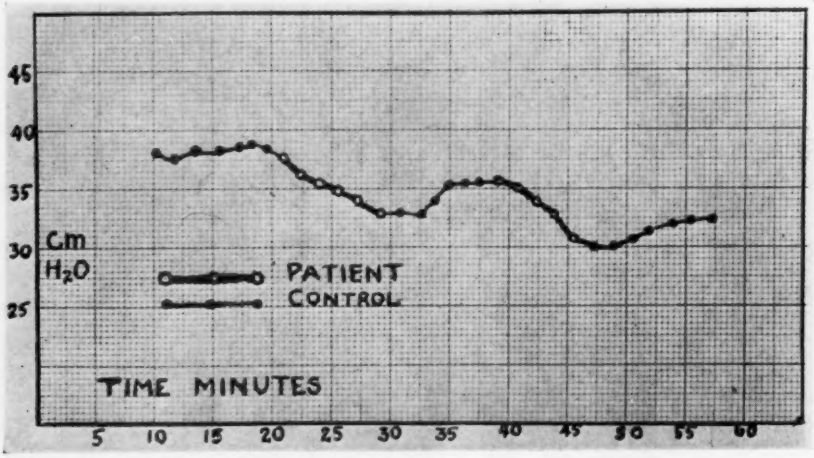


CHART 2.—Illustrating absence of pressor effect of patient's plasma following operative removal of tumor.

Postoperative Laboratory Data.—The basal metabolic rate on two occasions was minus 1 and 17. Chemical examination of the blood disclosed a fall of the urea to 11 mg. The blood sugar was 75 mg., and the total cholesterol had fallen to 270 mg. The blood count showed a moderate secondary anemia. The electrocardiogram was

unchanged. Oscillometric measurements still showed a diminution of peripheral pulsations, but they were more marked than preoperatively. There was an increase in peripheral skin temperatures, as determined by the dermotherm. The Janney test showed a flat curve for the blood sugar. It was no longer possible to demonstrate the presence of the pressor substance on repeating the perfusion experiment (Chart 2).

The patient had become very greatly improved when discharged, her blood pressure ranging between 125 and 135 systolic and 85 to 95 diastolic. Occasionally she is troubled with Raynaud-like symptoms in hands and feet, especially on exposure to cold. She has not had any attacks of the type described preoperatively.

COMMENT.—A matter of academic significance is brought up by this case. Although the majority of authors have expressed the opinion that the hypertensive crises in these cases are due to hyperadrenalinemia, several, in recent publications, have questioned this association. Some have actually doubted the causal relationship between the paraganglioma and the coexisting hypertension. Many previous authors have expressed regret over the lack of a reliable method of demonstrating the presence of adrenalin in the blood. This case would appear to be the first instance in which this pressor substance has been demonstrated in the blood biologically. The reversal effect of ergotamine makes it practically certain that the pressor substance is adrenalin. Moreover, the absence of this substance from the blood after the removal of the tumor establishes, beyond doubt, the causal relationship of this neoplasm to the hyperadrenalinemia and the hypertensive crises.

CONCLUSIONS

(1) A case of pheochromocytoma of the adrenal gland associated with hypertensive crises, relieved by successful operative removal of the tumor, is presented. This represents the seventh case successfully operated upon.

(2) This is the first instance of pheochromocytoma with hypertensive crises in which a pressor substance (adrenalin) has been demonstrated in the circulating blood during a crisis.

(3) No conclusions are drawn regarding the association of hyperadrenalinemia and essential hypertension.

(4) The value of perirenal insufflation in the preoperative demonstration of the tumor site is emphatically illustrated by this case.

REFERENCE

[1] Kelly, H. M., Piper, M. C., Wilder, R. M., and Walters, W.: Proc. Staff Meet., Mayo Clinic, January 29, 1936.

THE SHELVING OPERATION IN THE TREATMENT OF NEGLECTED OR IRREDUCIBLE CONGENITAL DISLOCATED HIP

ALBERT R. SMITH, M.D.

IOWA CITY, IOWA

FROM THE DEPARTMENT OF ORTHOPEDIC SURGERY, SERVICE OF DR. ARTHUR STEINDLER, THE STATE UNIVERSITY OF IOWA HOSPITALS, IOWA CITY, IOWA

PART I

IN EVALUATING the results of any therapeutic procedure two criteria must be borne in mind if the analysis and conclusions are to be accurate. These are: (1) To what degree has the measure under consideration restored the anatomic and functional integrity of the part? (2) What would have been the probable end-result if nothing had been done?

In reconstructive surgery particularly it is essential that the end-results of untreated cases be known before we are justified in asking patients to submit to operation. In adults, of course, the end-result is usually self evident; and we need concern ourselves only with the first of the two criteria mentioned. When, however, we are confronted with the same or a similar surgical problem in a young child, the importance of the end-results in untreated cases assumes larger proportions.

When we restrict ourselves to the problem of the congenitally dislocated hip we find in the literature innumerable reports of the results of the several systems of regimen. The analyses and end-results reported are almost universally predicated on the degree of restoration of anatomic and functional integrity. The ultimate grouping of cases in such analyses naturally depends on the standards of excellence demanded by the conscience of the observer. Thus we have the conflicting reports of Lange, Annovazzi,[2] Becker,[5] and a host of others. In none of these, not even in the overwhelming series discussed by Annovazzi, is there any mention made of the untreated cases in the comparable age groups.

For this reason it is felt that a study of the symptoms and complaints of untreated cases of congenital dislocation of the hip is not without value. In this study 69 cases, from six to 59 years of age, were used. The data were drawn largely from hospital records and the answers to questionnaires. The division of these cases into age groups and patients with unilateral or bilateral luxation is presented in Table I.

Of the group 6–10 years, four had operative work done later (open reduction in two cases, plaster encasement in one, and skin traction in one). Three of the remaining five were given no treatment, and the other two were treated conservatively (*i.e.*, by means of a shoe lift or corset).

Submitted for publication August 25, 1936.

TABLE I

UNTREATED CASES

Age	Total Number	Unilateral	Bilateral	Subluxated
6–10	9	5	3	1
11–15	19	13	5	1
16–20	7	4	3	0
21–25	13	7	4	2
26–30	8	6	1	1
31–40	7	5	0	2
41–50	3	2	0	1
50 and above	3	1	0	2
Totals	69	43	16	10

Of the group 11–15 years, five had operative work done later (bilateral Lorenz bifurcations in two cases, open reduction in one, manipulation and plaster encasement in two). Six received no therapy, and eight were treated conservatively.

In these two groups, ages 6–15 inclusive, it is seen that nine were treated operatively. In these cases *the admission record and symptomatology prior to treatment only are used in the compilation of the data to be presented. It is obvious that the symptoms and physical findings of these patients formed the basis of the operative indication.*

Of the group 16–20 years, one had had a closed reduction bilaterally at the age of two, with subsequent dislocation. She has had no treatment since the age of five, when the right hip was subspinous and the left hip subluxated. She is now known to have gone nine years with the right hip so dislocated and the left subluxated.

Three of this group were not treated and three were treated conservatively.

Of the group 21–25 years, one had had five futile attempts at closed reduction in childhood with resorption of the head. She has been treated conservatively since. Two others had been treated elsewhere in early childhood—the exact therapy is unknown, but it is presumed to have been closed reduction. Both of these cases had an indisputable luxation when seen here. They were treated conservatively. One case had a subtrochanteric osteotomy because of a bad flexion contracture. One case, not included in the tabulated data, was complicated by poliomyelitis, the residua of which brought her here shortly after her attack at the age of 23. Six of the remaining patients were treated conservatively and three had no therapy.

All patients over the age of 25 were either treated conservatively by means of a shoe lift and corset or else were given no therapy. The total number of cases treated conservatively was 33; 21 patients received no therapy at any time.

The symptoms may be classified as, (1) objective; namely, limp, shortening, scoliosis, and lordosis; and (2) the subjective symptoms of pain, fatigue,

Annals of Surgery
July, 1927

TABLE II

FREQUENCY OF SYMPTOMS IN UNTREATED CASES

Unilateral Dislocation (Cases 43)

Ages	Total No. of Cases	Limp	Shortening	Scoliosis	Lordosis	Pain				Fatigue			Stiffness
							Hip	Knee	Back		Hip	Back	
6–10.....	5	5	4	1	1	0				2	2	1	4
11–15.....	13	13	11	5	2	6	6	0	1	3	3	1	7
16–20.....	4	4	4	1	1	4	4			1	1		4
21–25.....	7	7	6	1	0	4	4	1		3	3		3
26–30.....	6	6	6	3	1	1	1			3	3		2
31–40.....	5	5	4	3	1	3	3	1		3	3		2
41 and above	3	3	3	1	1	3	3	2	3	3	3	3	2

TABLE III

FREQUENCY OF SYMPTOMS IN UNTREATED CASES

Bilateral Dislocation (Cases 16)

Ages	Total No. of Cases	Limp	Shortening	Scoliosis	Lordosis	Pain				Fatigue			Stiffness
							Hip	Knee	Back		Hip	Back	
6–10.....	3	3	1	0	3	0				1	1		2
11–15.....	5	5	1	1	5	3	2	1	1	3	3	1	4
16–20.....	3	3	1	2	1	1	1		1	2	2		1
21–25.....	4	4	0	0	1	3	3	1	2	2	2		4
26–30.....	1	1	1	0	1	1	1			1	1		0
Totals...	16	16	4	3	11	8	7	2	4	9	9	1	11

TABLE IV

FREQUENCY OF SYMPTOMS IN UNTREATED CASES

Subluxated (Cases 11)

Ages	Total No. of Cases	Limp	Shortening	Scoliosis	Lordosis	Pain				Fatigue			Stiffness
							Hip	Knee	Back		Hip	Back	
6–10.....	1	1	0	0	0	0				0			0
11–15.....	1	1	0	0	0	0				1	1		0
16–20.....	0	0	0	0	0	0				0			0
21–25.....	2	2	0	0	0	2	2			2	2		2
26–30.....	1	1	1	1	0	1	1			1	1	1	1
31–40.....	2	2	2	1	1	2	2	1	1	2	2		2
41 and above	3	3	3	1	1	1	1		1	3	3	1	3
Totals...	10	10	6	3	2	6	6	1	2	9	9	2	8

and stiffness. Their frequency in the various age groups is shown in Tables II, III and IV.

The tables show a marked discrepancy between the number of patients complaining of shortening and the number admitting a scoliosis. Of the symptoms tabulated by far the most reliable are those of limp, shortening and pain. The last named with its counterpart fatigue is frequently the cause of the older children and adults seeking amelioration of their ailment. With respect to pain alone in the unilateral cases it is noted that no patient complained of pain before the tenth year. (Two, however, gave a history of easy fatigability. In only two other instances was fatigue admitted without pain in the unilateral cases; they were both in the age group 26–30). The development of this symptom complex (pain-fatigue) is shown in Table V.

TABLE V

FREQUENCY OF PAIN-FATIGUE IN UNTREATED CASES OF CONGENITAL DISLOCATED HIP

Unilateral

Age	No. Cases	Pain or Fatigue
6–10	5	2 or 40%
11–15	13	6 or 46%
16–30	17	11 or 64.7%
31 and above	8	6 or 75%

Above the age of 40 all three patients complained of pain and fatigability in the hip.

In the bilateral cases the series is so small that the percentages are rather meaningless. However, in these instances fatigue but no definite pain occurred more frequently than in the unilateral group; namely, once in each age group up to 20 years. The development of pain-fatigue in the bilateral cases is shown in Table VI.

TABLE VI

FREQUENCY OF PAIN-FATIGUE IN UNTREATED CASES OF CONGENITAL DISLOCATED HIP

Bilateral

Age	No. Cases	Pain or Fatigue
6–10	3	1 or 33.33%
11–15	5	4 or 80%
16–30	8	6 or 75%

Four of the five bilateral cases over 20 complained of both severe pain in the hips and low exercise tolerance.

These results are quite the reverse of those reported by Colonna[9] who found that "Pain is rarely a symptom except when there was present in the adult patient some degree of arthritis. Most common is that of easily fatigued, combined with the characteristic limp such as would be caused by a shortened and unstable extremity." These results more closely agree with those found by Gill,[22, 23] or those reported by Øwre[30] in his study of the subluxated hip.

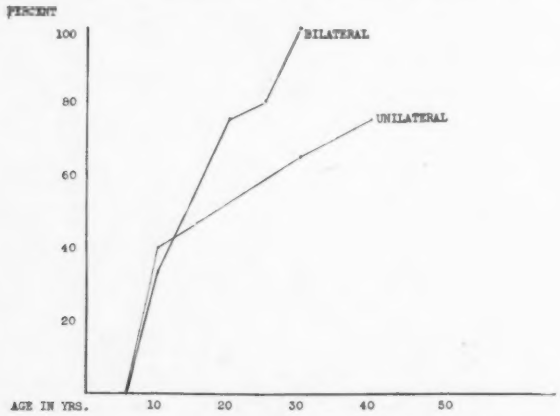
In recapitulation, it would seem that a child with unilateral dislocation of

the hip has a good chance of reaching the fifteenth year with no complaint other than that of limp and unsightly gait. From then until the thirtieth year the probabilities are somewhat in favor of his developing pain or fatigability. Above 30 it seems certain that pain will appear, the exact age and degree depending on the degree of arthritis.

The bilateral cases, on the other hand, can be expected to get along only until they reach the tenth year before paying the price of their mechanically expensive gait; and by the time such a patient has reached the twentieth year of life he is practically certain to have pain and fatigue (Chart I).

CHART I

COMPARISON OF THE FREQUENCY OF PAIN-FATIGUE IN THE UNILATERAL AND BILATERAL UNTREATED CASES



THE PALLIATIVE OPERATIONS

(1) Shelving.—The question of whether or not the palliative procedures of shelving or the Lorenz-Baeyer bifurcation or Schanz operations ameliorate the symptoms of these neglected cases now presents itself. We are not concerned with either the use of the shelving operation as an adjunct to open reduction, or the use of it and the bifurcation operation in other conditions; but only their applicability as a palliative measure in the congenitally dislocated hip. Within this narrow field 28 shelving operations have been performed here since 1925, on 25 patients (Table VII).

TABLE VII

SHELVING OPERATIONS

Age	No. Cases	Unilateral	Bilateral	Subluxated
6–10	12	4	8	0
11–15	6	6	0	0
16–20	5	4	0	1
21 and above	2	0	0	2
Totals	25	14	8	3

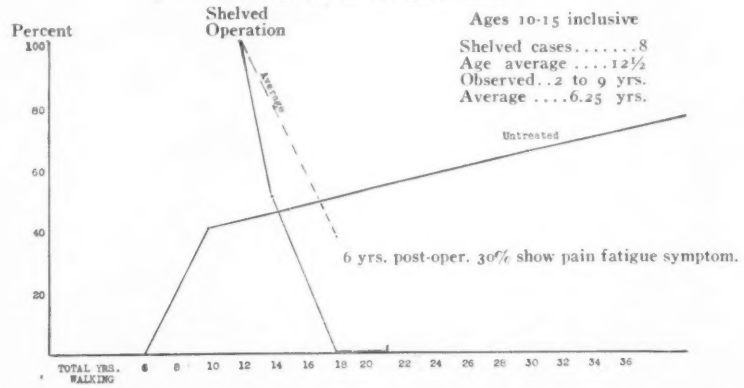
In the first group 6–10 years old, one bilateral case, shelved on one side, is too recent to be evaluated. This case is discarded. All the patients in this group were treated first by attempts at closed reduction and in most instances several such attempts at reduction were made before deciding on open operation.

Here, also, in a few instances shelving was elected only after open reduction was found impossible at operation. In one case shelving was effected at a second sitting four months after an open reduction had been performed which failed to maintain reduction.

In the bilateral group four were shelved on one side and three were shelved on both sides, making a total of ten hips. The finale ultima of these hips will be discussed later.

CHART II

COMPARATIVE FREQUENCY OF PAIN-FATIGUE IN UNTREATED AND IN SHELVED CASES



A 36 year old patient with bilateral subluxated hips had a shelving effected on one side only, the right. One year later a reconstruction and arthroplasty on the opposite hip was performed. However, during this interval she had so much difficulty and pain in the left hip that she was scarcely ambulatory. This case is also discarded.

There remains then a total of 23 patients with 26 hips which were shelved and are now available for analysis.

The remainder of the patients differ only as to observation time and age. Nearly all had had attempts at closed reduction in childhood and in all the shelving was the first open work attempted on the joint. Tables VIII, IX, X and XI show the symptomatic results by age groups.

The symptoms of pain and fatigue are a function of the activity of the patient. That is to say, a patient who never walked would not be troubled by a congenital dislocation of the hip. Hence, in comparing the frequency of these symptoms in the treated and the untreated cases, we compare them in terms of years of walking, with and without shelves, respectively.

It does not logically follow that simply because a patient's symptoms have

TABLE VIII

FREQUENCY OF SYMPTOMS IN SHELVED CASES

Fourteen Unilateral Cases

Ages	Total No. of Cases	Observ. Period (in Yrs.)	Limp	Shortening	Symptoms—Postoperative				
					Scoliosis	Lordosis	Pain	Fatigue	Stiffness
6–10	4	2–9, average 3.75	4	3	1	2	0	1, but this is markedly decreased	0
11–15	6	2–9, average 6	6	5	6	3	1, but this is much less than before	2	1
16–20	4	3–7, average 4.8	4, decreased in 3	4, decreased in 1	2	1	1, much less than before	3, much less than before	0

TABLE IX

FREQUENCY OF SYMPTOMS IN SHELVED CASES, ONE SIDE ONLY SHELVED

Four Bilateral Cases

Case	Age at Time of Shelving (in Yrs.)	Observ. Period (in Yrs.)	Limp	Shortening	Symptoms—Postoperative					Status of Other Hip
					Scoliosis	Lordosis	Pain	Fatigue	Stiffness	
H. P.	8	1	Yes	Yes	Yes	Yes	No	No	No	Open red. without shelf
M. B.	6	1½	Yes	Yes	No	No	No	Yes	Yes	Disloc. at end of observ. period. Bifurcation 3 mos. later. Shelved side bifurcated
A. L.	7	1	Yes	Yes	No	No	No	Yes	Yes	Closed—poor result. Bifurc. on shelved side at end of observ. time
R. W.	10	1½	No	Yes	No	No	No	No	No	Cl. reduct. Excellent result
Totals 4			3	3	1	1		2	2	

been relieved after a shelving operation, the shelf built is the cause of the improvement. To so consider things is *post hoc ergo propter hoc* reasoning. The operative trauma alone, even though the joint is not opened, will result in sufficient scarring about the joint to limit the excursion of the femur upward and thus result in some increased stability. The weeks and months of physical therapy necessary to restore full motion after a simple shelving attest to this. If, however, after the complete mobilization of the joint we find that the symptoms of patients are relieved in the presence of a good shelf and are not relieved in those in whom a good shelf is absent, then we are justified in the belief that the shelf is the cause of the improvement (Chart II).

Analysis of the patients in the younger group especially shows that the shelving operation is far from the panacea it is sometimes considered. Here, all too often further operative work is demanded; and here also we find that the shelf, although present, may be nonfunctional (Tables XII and XIII).

TABLE X

FREQUENCY OF SYMPTOMS IN SHELVED CASES, BOTH SIDES SHELVED

Three Bilateral Cases

Case	Age (in Yrs.)	Observ. Period (in Yrs.)	Limp	Short-ness	Symptoms—Postoperative				
					Sco-liosis	Lor-dosis	Pain	Fa-tigue	Stiff-ness
F. N.	6	1½	Yes	No	Yes	No	No	No	Yes
		1¼							
P. A.	7	2	Yes	Yes	No	No	No	Yes	No
		1							
F. P.	9	4¼	Yes	No	No	No	No	No	No
		3							
Totals	3		3	1	1	None	None	1	1

TABLE XI

FREQUENCY OF SYMPTOMS IN SHELVED CASES, UNILATERAL

Two Subluxated Cases

Case	Age (in Yrs.)	Observ. Period (in Yrs.)	Limp	Short-ness	Symptoms—Postoperative				
					Sco-liosis	Lor-dosis	Pain	Fa-tigue	Stiff-ness
G. R.	20	3	Yes (de-creased)	Yes	No	No	Rare	De-creased	No
J. S.	27	10	Yes	No	No	No	No	No	Slight
Totals	2		2	1	None	None			

Thus we see in the unilateral cases that in only two out of the 12 shelvings (16 per cent) done after the age of 10 was a secondary operation performed; and in only three instances (25 per cent) was such an indication made. This is in striking contrast to the younger age group where two out of the four unilateral cases demanded a secondary osteotomy and one of the remaining two was developing genu valgum when last seen.

TABLE XII

OPERATIONS SUBSEQUENT TO SHELVING

Sixteen Unilateral Cases

Age Group	Total No. of Cases Shelved	Operation Subsequent to Shelving	Indication for Second Operation
6–10	4	Osteotomy in *two* cases	Poor position—adduction in one 30° flexion contr. in the other
11–15	6	None	
		Bifurcation—this was advised in one case because of instability. Operation refused. Pt. now 5 yrs. post-shelving. She is unaware of any instability or loss of motion or limp	
16–20	5 (one case of subluxation)	Resection of part of shelf	This was done in the case of subluxation because of persistent pain and presence of a very long shelf. Pt. now symptom free
		Osteotomy and lengthening of tendo achillis	50° flex. contr. and equinus of foot secondary to that contracture
Above 20	1	None	

TABLE XIII

OPERATIONS SECONDARY TO SHELVING

Six Bilateral Cases

Age Group	Total No. of Cases Shelved	Operation Subsequent to Shelving	Shelving Bi- or Unilateral	Indication for Secondary Operation
6–10	6	*A*—Repeat shelving	Bilateral	First hip shelved at age 7. Absorbed one year later
		B—Bifurcation	Unilateral—closed reduction on other side	Resorption of shelf with dislocation after one year
		C—Osteotomy	Unilateral—bifurcation on other hip	Done on shelved side because of resorption of shelf with redislocation
		Bifurcation	*Same patient as Case C*	Done on shelved side because of resorption of shelf with redislocation
		Fusion	*Same patient as Case C*	Shelved side finally fused because of malposition and marked disability

The bilateral cases are unfortunately all in the youngest age group. Here we find that three of the six cases, comprising 33 per cent of the hips shelved, required secondary operations.

TABLE XIV

ULTIMATE FATE OF THE SHELF AS SEEN ROENTGENOLOGICALLY

Thirteen Unilateral Cases

Case	Age at Time of Shelving (in Yrs.)	Time Elapsed Since Shelving (in Yrs.)	Roentgenologic Appearance of the Shelf
B. F.	4	2½	Poor shelf.* Shelf still present but nonfunctional. Pt. has a subtrochanteric osteotomy (Schanz) which supports the pelvis well. The plate taken 4 months postoperative shows a small shelf just covering the head. Hip very high and posterior
F. B.	4	1	Poor shelf. Immediate postoperative plate also shows a poor shelf
J. D.	10	4	Good shelf*
M. W.	10	2	Good shelf
C. B.	13	1	Good shelf
R. J.	15	6	Good shelf
N. B.	15	2	Good shelf
A. K.	16	3	Good shelf
G. D.	17	4	Fair shelf*
E. P.	18	4	Good shelf
G. K.	19	1	Good shelf
G. R.	20	3	Good shelf
J. S.	27	1	Good shelf

* A good shelf is defined as one of good density, closely applied to the head, and which covers it completely. A poor shelf is one far removed from the head (2½ cm., or more) and which does not cover 50 per cent of the head with the leg in neutral so far as abduction and adduction are concerned. A fair shelf is one falling between the above two.

TABLE XV

ULTIMATE FATE OF THE SHELF AS SEEN ROENTGENOLOGICALLY

Four Bilateral Cases

Case	Age at Time of Shelving (in Yrs.)	Time Elapsed Since Shelving	Roentgenologic Result	Status of Other Hip
H. P.	8	½ yr.	Fair	Excellent result of open reduction since shelving
M. B.	6	1 mo.	Good	Closed reduction. Redislocated after the shelving. Remained luxated until 2 yrs. postbifurcation.
		1 yr.	Shelf partially absorbed.	
		2 yrs.	Fair. *Remaining spicule detached. This pt. finally came to fusion.*	
A. L.	7	3 mos.	Poor shelf	Closed reduction Fair result
		8 mos.	Shelf completely absorbed	
R. W.	10	1½ yrs.	Good shelf	Closed reduction Excellent result

It remains now to report on the roentgenologic or anatomic results. The ultimate fate of the shelf as seen roentgenologically closely parallels the results found clinically. Table XIV shows the final anatomic outcome in the various age groups. Unfortunately, in only 20 of our original 23 cases are roentgenograms now available taken one year or more after the shelving.

Thus in 13 unilateral cases with observation time from one to six years, ten or 76.9 per cent are anatomically good results, one or 7.6 per cent are fair results, making a total of 84.5 per cent satisfactory shelves.* It is to be noted that all shelves classified as good are in patients who at the time of operation were 10 years old or more. This high percentage of satisfactory shelves is quite the reverse of Ober's[29] findings inasmuch as he reports that "50 per cent of the shelves absorb."

In the bilateral cases the patients are divided into those having one side shelved and those having both sides shelved (Tables XV and XVI).

TABLE XVI

ULTIMATE FATE OF THE SHELF AS SEEN ROENTGENOLOGICALLY

Three Bilateral Cases

Case	Age at Time of Shelving (in Yrs.)	Time Elapsed Since Shelving	Roentgenologic Appearance of the Shelf
F. N.	6	1 yr. for both hips	Fair on the right (first hip shelved) and poor on the left
P. A.	7	2 yrs. and 1 yr., resp.	The first shelf is now absorbed. There is a good shelf on the opposite side (right)
F. P.	9	4½ yrs. and 3 yrs., resp.	There is a good shelf present bilaterally

Thus the results in the bilateral cases are much poorer than those found in the unilateral patients. In those cases with but one side shelved there are only two shelves that could be classified as good (50 per cent); and one of these ultimately absorbed and the patient finally had a fusion of that hip. One of the other two cases which had but one side shelved had a poor shelf to start with, which after eight months was completely resorbed. The remaining case has a fair shelf, but the observation time is only six months. There is just one case with a good shelf at the end of one year observation period.

The bilateral luxations on whom both sides were shelved fared slightly better. Here only one shelf is absorbed after an observation period of two years, while the other side which has been followed for one year can still be classified as good. Only one poor shelf is present in this group of six hips.

Combining the anatomic findings with the functional results shows how closely the final end product parallels the anatomic result (Tables XVII, XVIII and XIX).

In analyzing these results it is necessary to discard those cases in which a secondary osteotomy was performed and the functional improvement noted is due to the combination of operations. Those instances where the poor results

* NOTE.—Since this data was tabulated patient H. T. has returned to clinic. The anatomic result is shown in the illustration. The functional result is excellent.

FIG. 1.—Case J. S., shelved at age of 27. Roentgenogram shows anatomic result ten years postoperative.

FIG. 2.—Case H. T., shelved at age of 11. Roentgenogram shows result seven years postoperative.

FIG. 3.—Case M. W., shelved at age of 10. Roentgenogram shows result two years postoperative.

TABLE XVII

FUNCTIONAL RESULTS IN SHELVED CASES CORRESPONDING TO VARIOUS ANATOMIC FINDINGS

Thirteen Unilateral Cases

Case	Age at Time of Oper. (in Yrs.)	Functional Result	Observ. Period (in Yrs.)	Anatomic Result	Observ. Period (in Yrs.)
B. F.	4	Unknown—never ambulatory. Since osteotomy it is fair	2½	Poor	2½
F. B.	4	Poor*	1	Poor	1
J. D.	10	Good*	9	Good	4
M. W.	10	Poor prior to osteotomy. Good since	2	Good	2
C. B.	13	Poor—wears a corset	9	Good	1
N. B.	15	Good	2	Good	2
R. J.	15	Good	8	Good	6
A. K.	16	Poor prior to osteotomy. Good since	7	Good	3
G. D.	17	Fair*	5	Fair	4
E. P.	18	Good	4	Good	4
G. K.	19	Good	1	Good	1
G. R.	20	Good	3	Good	3
J. S.	27	Good	10	Good	1

* A good functional result is one which does not fatigue easily, in whom the Trendelenburg is slight or absent, and who has 60° flexion and 20° abduction and only slight limp. A fair result is one who does not fatigue as easily as before, in whom the limp is decreased, and who has painless motion of at least 40° flexion. A poor result is one in whom the operation has either made no change in the symptoms or has aggravated them.

TABLE XVIII

FUNCTIONAL RESULTS IN SHELVED CASES CORRESPONDING TO VARIOUS ANATOMIC FINDINGS

Four Bilateral Cases

Case	Age at Time of Oper. (in Yrs.)	Functional Result	Observ. Period (in Yrs.)	Anatomic Result	Observ. Period	Status of Other Hip
H. P.	8	Good	1	Fair	6 mos.	Open reduction Excellent result
M. B.	6	Poor	2	Poor	2 yrs.	Bifurcation
A. L.	7	Poor	1	Poor	1 yr.	Reduction (closed)
R. W.	16	Good	1	Good	1 yr.	Reduction (closed)

TABLE XIX

FUNCTIONAL RESULTS IN SHELVED CASES CORRESPONDING TO VARIOUS ANATOMIC FINDINGS

Three Bilateral Cases

Case	Age at Time of Oper. (in Yrs.)	Functional Result		Observ. Period (in Yrs.)	Anatomic Result	Observ. Period (in Yrs.)
F. N.	6	Good	rt.	1	Fair	1
		Poor	lt.	1	Poor	1
P. A.	7	Good	rt.	1	Good	1
		Poor	lt.	2	Poor	2
F. P.	9	Good	rt.	1	Good	1
		Good	lt.	5	Good	3

In a few instances the observation period for the functional result is much greater than that for the anatomic result in the same case. This is made possible by the fact that the functional result is predicated on the answers to a questionnaire in addition to the hospital record. The anatomic result, of course, is based entirely on the roentgenologic appearance and hence the observation time may be shorter than in the functional results, since the patient was not available for further roentgenologic studies

of the shelving led to a procedure of greater magnitude or to one with the same objective, namely, to support the pelvis (*viz.*, Schanz osteotomy, bifurcation, and fusion) must be included. Thus we have 11 patients for study in the unilateral cases. Here we find seven with good functional results having seven good anatomic results. There is one poor functional result having a good anatomic result. The two patients having only a fair functional result had, likewise, only a fair anatomic result. There remains one patient in whom the functional result is unknown but who had a poor shelf, and one patient with a poor shelf and a poor functional result. Thus, in 80 per cent the functional and anatomic result was satisfactory. Again, attention is called to the fact that all good functional results, like the good anatomic results, are in patients ten years old or over.

In the bilateral cases who had only one side shelved we find two good functional results in which there were a good and a fair shelf present, respectively. The two poor functional results had likewise poor shelves.

In the bilateral cases with both sides shelved we find that the functional results are identical with the anatomic findings except in one hip where there was fair function and a good shelf.

Thus it is seen that a good functional result depends primarily on the building of an adequate shelf at operation. The high percentage of failures in the younger age group, however, seems to show that the prognosis of the functional value of a shelf built before the tenth year is precarious, to say the least.

THE LORENZ-BAEYER BIFURCATION.—The cases in which the bifurcation has been adopted as the procedure of first choice are only three in number, two of which are available for analysis. These are both bilateral cases, ages 12 and 14, respectively. One (age 12) had the bifurcation on both sides, while the other, complicated by spastic paralysis, had it only on one side. In addition to these patients there are the two patients who had the bifurcation following an unsuccessful shelving. One of these (A. L.) had the bifurcation on the one (previously shelved) side only. The other (M. B.) had bilateral bifurcation operations.

TABLE XX

FREQUENCY OF SYMPTOMS IN CASES OF BILATERAL DISLOCATION WITH BIFURCATION OSTEOTOMY

Two Cases with Bifurcation on One Side Only

Patient	Age at Oper. (in Yrs.)	Observ. Period (in Yrs.)	Limp	Shortening	Symptoms—Postoperative				
					Scoliosis	Lordosis	Pain	Fatigue	Stiffness
V. H.	14	4	Decreased	Yes	No	No	Rare	Slight	No
A. L.	8	1	Yes	Yes	No	No	No	No	No

Thus there is a total of five patients, all with bilateral dislocations, with eight bifurcation operations. Four of these patients with six bifurcations are available for study. The frequency of symptoms in the individuals is given in Tables XX and XXI.

TABLE XXI

FREQUENCY OF SYMPTOMS IN CASES OF BILATERAL DISLOCATION WITH BIFURCATION OSTEOTOMY

One Case with Bifurcation on Both Sides

Patient	Age at Oper. (in Yrs.)	Observ. Period (in Yrs.)	Limp	Shortening	Symptoms—Postoperative				
					Scoliosis	Lordosis	Pain	Fatigue	Stiffness
M. B.	8	3	Yes	Yes	No	No	No	Yes	Slight on first side operated

Thus it is seen that in only one case was pain present following the bifurcation. This represents 16 per cent of the hips operated upon, and compares favorably with the results of the shelving operation.

Øwre reports that the bifurcation is best not done until the fifteenth year or later because of the loss of the supporting angle in the younger cases. The ultimate fate of this angle in our cases is given in Table XXII. Three of the patients comprising five of the total six hips are available for roentgenographic analysis.

TABLE XXII

THE ULTIMATE FATE OF THE SUPPORTING ANGLE IN CASES WITH BIFURCATION

Three Bilateral Cases

Patient	Age at Oper. (in Yrs.)	Observ. Period	Bifurcation Bi- or Unilateral	X-ray Appearance of Supporting Angle
A. L.	8	1 yr.	Unilateral. Other hip reduced by closed meth.	3 mos. p.o. plate shows good carrying angle. Serial plates throughout observ. period show a progr. loss of this angle. At end of year, however, there is still good support afforded the pelvis
M. B.	8	1 yr., 9 mos.	Bilateral	After 1 yr. angle in first hip operated good. After 9 mos. angle in second hip good but there is marked add. deformity
M. M.	12	1½ yrs.	Bilateral	Good supporting angle abutting against pelvis nicely on both sides

Thus we see that at the end of the first year at least the bifurcation operation still affords the pelvis good support. This series of hips, however, is too small and the observation periods altogether too short to warrant any

definite conclusions in this matter. The number of hips requiring secondary surgical procedures following the bifurcation operation in these patients is also distressingly high, just as it is in the cases with bilateral dislocation of the same age period which were shelved. The incidence of secondary operative work done in these individuals who had the bifurcation operation is shown in Table XXIII.

TABLE XXIII

OPERATIONS SUBSEQUENT TO BIFURCATION

Four Bilateral Cases

Patient	Age at Time of Bifurc. (in Yrs.)	Time Elapsed Prior to Secondary Operation	Bifurcation Bi- or Unilateral	Secondary Operation	Indications for Secondary Operation
V. H.	14		Unilateral; other hip not treated	*None*	
A. L.	8	8 mos.	Unilateral;	Supracondylar osteotomy	Genu valgum. (This hip was previously shelved)
		1 yr.	clos. reduct. on other side	Supracondylar osteotomy	Prev. osteotomy resulted in poor position. Second osteotomy necessary only by virtue of error in technic
M. M.	12		Bilateral	*None*	
		9 mos.	Bilateral	Adductor tenotomy	Adduction deformity. (This hip was previously shelved)
M. B.	8	1½ yrs.		Subtroch. osteotomy	Adduction contracture. (This is the same hip as above)
		2 yrs., 7 mos.		*Fusion*	*Originally shelved hip finally fused because of poor position (adduction) and instability*

Thus here, as in the cases with bilateral dislocation in whom shelving operations were performed, 33 per cent of the hips treated by bifurcation required further surgical procedures.

In correlating the anatomic findings with the functional results we find that the patients who did not require further operative work and in whom the anatomic results are good have also good functional results. One of these (V. H.), with a unilateral bifurcation, is able to carry on farm work, and does not consider himself disabled. The two patients in whom osteotomies were necessary after the bifurcation had poor functional results up to the time of the osteotomy. The convalescent period subsequent to the osteotomy is not yet passed in either individual.

Table XXIV gives the comparative frequency of symptoms in cases with a bilateral dislocation which were shelved, and those on whom a bifurcation operation was performed. No regard has been paid to whether either operation was performed on one or both sides. The percentage figures represent the percentage of hips operated upon in the respective group. The combined group age range was 6 to 12 years.

TABLE XXIV

COMPARATIVE FREQUENCY OF SYMPTOMS IN CASES WITH BILATERAL DISLOCATION HAVING SHELF OR BIFURCATION OPERATION

Operation	Symptoms—Postoperative				Observation Time
	Limp	Pain	Fatigue	Stiffness	
Shelf (10 hips)	9 or 90%	*None*	3 or 33%	2 or 20%	1–4 yrs., average 1.85 yrs.
Bifurcation (6 hips)	6 or 100%	1, but this was rare (16%)	3 or 50%	3 or 50%	1–4 yrs., average 2.96 yrs.

Thus it is seen that the symptom complex, pain-fatigue, was present in four of the six hips (66 per cent), in which a bifurcation had been performed, while of the ten hips shelved only three (33 per cent) complained of either pain or fatigue. As we have seen previously in both groups of cases, a third of the hips operated upon required secondary surgical work.

SCHANZ OSTEOTOMY.—The Schanz or low osteotomy has been performed in only two instances of congenital dislocation of the hip in this clinic. One of these was bilateral and had the operation on both sides; the other was a case of unilateral luxation and the Schanz osteotomy was secondary to a shelving procedure.

As Gaenslen[19] points out, the difficulties following bilateral operation in double dislocation are due to bilateral insufficiency of the glutei. In the case on whom bilateral Schanz osteotomies were performed the patient had nothing but pain and distress from the procedure. A shelving was effected later with marked relief—so much so that she requested that the other side be shelved.

The other patient had the Schanz osteotomy following a shelving operation which had failed to give him any benefit. He has been considerably improved so far as limp, pain, fatigability and gait are concerned.

CONCLUSIONS

The data show that the unilateral case has a good chance to reach the age of 15 without the hip causing marked symptoms or disability. This is probably simply a manifestation of the well known fact that the victim of a chronic disease in early life learns how to live with his ailment and stays within the bounds of whatever restriction it imposes. So far as the unilateral congenital dislocation of the hip is concerned, it is most unlikely that such a patient can

reach the age of 40 without being forced to seek medical aid, regardless of how much he restricts his activities.

The bilateral case, on the other hand, can hardly be expected to reach the tenth year before complaining of pain or fatigue. It is almost certain that before arriving at the age of 20 such a patient will have pain and disability.

The palliative procedure of shelving is seen to ameliorate these symptoms to a marked degree, especially in the older children with a unilateral dislocation. This benefit has been known to last at least nine years. From our data the operation described by Herbst[24] and reported in greater detail by Deutschländer[13] does not appear to be justified. The same impression is created by the reports of the experiences of other American observers, such as Gill[22, 23] or Dickson,[14] who finds 82.2 per cent of the shelvings give satisfactory results.

The functional efficacy of the shelf operation is markedly reduced in the younger cases and in the patients with a bilateral dislocation. Here the number of patients requiring secondary surgical procedures on the shelved side is comparatively high.

The cases on whom the bifurcation operation has been performed are too few in number to warrant any far-reaching conclusions. However, in our small series this procedure has not controlled the symptoms of limp, pain, fatigue and stiffness as well as the shelving has done in the comparable age groups.

Our experience with the Schanz osteotomy in congenital dislocation of the hip is too limited to permit analysis.

REFERENCES

[1] Allison, N. A.: The Adaptive Changes in the Hip in Congenital Dislocation and Their Importance in Treatment. Jour. Bone and Joint Surg., **10,** 687.

[2] Annovazzi, G.: Congenital Dislocation of the Hip. Results of the Bloodless Method. (Trans. by A. Steindler.) Arch. di Ort., March, 1933.

[3] Baj, L.: Early and Late Changes after Reduction of Congenital Dislocation of the Hip. (Trans. by A. Steindler.) Arch. di Ort., **49,** 2.

[4] Beck, H.: Zur Frage der Unblutigen Behandlung der Angeborenen Hüftgelenksverrenkung. Deutsch. Ztschr. f. Chir., **243,** 723.

[5] Becker, F.: Beiträge zum Endergebniss der Unblutig Behandelten Angeborenen Hüftgelenksluxation. Deutsch. Ztschr. f. Chir., **241,** 273.

[6] Böhm, Max: Investigations into the Development of the Hip Joint and the Pathogenesis of So Called Congenital Dislocation of the Hip. (Trans. by A. Steindler.) Ztschr. f. Orth. Chir., **60,** 401.

[7] Brolin, J.: Review of Old Congenital Dislocation Treated by Subtrochanteric Osteotomy at Gottenburg Orth. Hosp. Acta Orthop., Scand., **5,** 109.

[8] Camitz, H.: On the Bifurcation Operation by the Baeyer-Lorenz Procedure and the Low Osteotomy of Schanz. Acta Orthop. Scand., **5,** 261.

[9] Colonna, Paul: Congenital Dislocation of the Hip in Older Subjects. Jour. Bone and Joint Surg., **14,** 277.

[10] Compere, E. L., and Phemister, D. B.: The Tibial Peg Shelf in Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17,** 60.

[11] Dega, W.: Spontanheilung der angeb. Hüftgelenkluxation Zugleich ein Beitrag zur Pfannendachplastik. Ztschr. f. Orth., **64,** 145.

[12] Dega, W.: Anatomy and Mechanics of Foetal Hip Studied in Order to Clarify Aetiology and Pathogenesis of Congenital Dislocation of the Hip. (Trans. by E. Freund.) Chir. d. Org. di Movemento, **18,** 425.

[13] Deutschländer, C.: Erfahrung über die Radikaloperation der Angeborenen Hüftverrenkung bei Erwachsenen. Deutsch. Ztschr. f. Chir., **232,** 52.

[14] Dickson, F. D.: The Shelf Operation in the Treatment of Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17,** 43.

[15] Doran, W. G.: Early Symptoms of Congenital Dislocation of the Hip Joint. Jour. Med. Soc. N. J., **29,** 564.

[16] Faber, Alex.: Zur Prognose der Unblutig Reponierten Angeborenen Hüftluxation. Ztschr. f. Orth. Chir., **62,** 359.

[17] Farrell, B. P., and Howorth, M. B.: Open Reduction in Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17,** 35.

[18] Freiberg, A. H.: Congenital Luxation of the Hip. Jour. Bone and Joint Surg., **17,** 1.

[19] Gaenslen, F. J.: Schanz Subtrochanteric Osteotomy for Irreducible Dislocation. Jour. Bone and Joint Surg., **17,** 16.

[20] Gaugele-Kienzle: Die Erfolge bei der Behandlung der Sogenannten Angeborenen Hüftgelenksverrenkung. Deutsch. Ztschr. f. Chir., **245,** 214.

[21] Gichler, H.: Ein Beitrag zur Frage der Luxatio Coxae Congenita. Arch. f. Orth. u. Unfall Chir., **33,** 248.

[22] Gill, A. B.: Operation for Old or Irreducible Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **10,** 696.

[23] Gill, A. B.: Plastic Construction of the Acetabulum in Congenital Dislocation of the Hip. The Shelf Operation. Jour. Bone and Joint Surg., **17,** 48.

[24] Herbst: Die Blutige Einrenkung der Angeborenen Hüftgelenkluxation. Deutsch. Ztschr. f. Chir., **217,** 359.

[25] Howorth, M. B., and Smith, H. W.: Congenital Dislocation of the Hip Treated by Open Operation. Jour. Bone and Joint Surg., **14,** 299.

[26] Howorth, M. B.: Shelf Stabilization of the Hip. Jour. Bone and Joint Surg., **17,** 945.

[27] Kidner, F. C.: Comparative Analysis of the Results of Open and Closed Reductions in Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17,** 25.

[28] Lowendorf, C. S.: The Bifurcation Operation. Jour. Bone and Joint Surg., **15,** 493.

[29] Ober, F. R.: Shelf Operation to Relieve Persistent Dislocation of the Hip. Jour. Bone and Joint Surg., **17,** 73.

[30] Øwre, Axel: Painful Congenital Subluxation of the Hip. Acta Chir. Scand., **76,** 369.

[31] Putti, V.: The Early Treatment of Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **15,** 16.

[32] Schede, F.: Zur Frage der Ergebnisse der Reponierten Hüftluxation. Arch. f. Orth. Chir., **60,** 474.

[33] Steindler, A., Kulowski, J., and Freund, E.: Congenital Dislocation of the Hip. J.A.M.A., **104,** 302.

[34] Swett, P. P.: An Operation for the Reduction of Certain Types of Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **10,** 675.

[35] Tillmans, W.: Die Kongenitalen Hüftluxationen. Deren Behandlung und Ergebnisse. Ztschr. f. Orth. Chir., **53,** 52.

(*To be continued*)

THE TOXIN OF BURNS

SOL ROY ROSENTHAL, M.D., Ph.D.

CHICAGO, ILL.

FROM THE DEPARTMENTS OF THERAPEUTICS AND BACTERIOLOGY OF THE UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE, CHICAGO, ILL.

THE theories explaining the toxic manifestations following extensive burns are (Harkins[4]):

(1) *Physical,* in which there is a local leakage of plasma into the tissues altering the circulation and resulting in a diminished blood volume, a diminished cardiac output, and finally a collapse of the blood pressure (the diminished blood volume is accompanied by an increased concentration of blood and hemoglobin).

(2) *Toxic,* whereby the supposed toxemia caused by the burn results, after a certain time, in shock and death.

Whereas the earlier authors (Parascandolo,[12] Pfeiffer,[14] Lewis and Grant[9]) demonstrated the presence of a toxic substance in the blood of burned individuals (later Robertson and Boyd,[15] Shimada,[17] Nagamitu[10]), the more recent authors question the presence of a toxin (Harrison and Blalock,[7] Harkins,[5] Wilson and Stewart, Underhill and Kapsinow[18]). Indeed, Underhill and Kapsinow emphasized that as long as we entertain the idea of a burn toxin, the progress in the understanding of burns and its therapy will be delayed.

One of the important factors in the modern concept of the pathogenesis in burns (and traumatic shock) is that there is a local accumulation of fluid which begins immediately or shortly after the injury, and continues thereafter, resulting in a decrease of the blood volume and an increase in the blood concentration. According to Harkins and others, if the process is too severe, the cardiac output decreases, and when this reaches one-third its normal, the blood pressure falls and death ensues as a result of cardiac failure—secondary shock (Underhill, Kapsinow and Fisk, Blalock, Harkins for burns; and Roome, Keith and Phemister,[16] Parsons and Phemister[13] for traumatic shock).

The protagonists of the toxic theory have offered many possibilities as to the nature of this toxin. Parascandolo links it to the ptomaines. Pfeiffer believes it resembles the nucleoproteins of snake venom. Robertson and Boyd believe it to be primary and secondary proteoses. The latest concept is that it is histamine-like in character because it effects a drop in blood pressure (rabbits and cats), and it contracts smooth muscle (uterus, intestinal strip—Shimada, Nagamitu).

The following experiments were undertaken to determine whether or not

Submitted for publication December 23, 1936.

[12] Dega, W.: Anatomy and Mechanics of Foetal Hip Studied in Order to Clarify Aetiology and Pathogenesis of Congenital Dislocation of the Hip. (Trans. by E. Freund.) Chir. d. Org. di Movemento, **18**, 425.

[13] Deutschländer, C.: Erfahrung über die Radikaloperation der Angeborenen Hüftverrenkung bei Erwachsenen. Deutsch. Ztschr. f. Chir., **232**, 52.

[14] Dickson, F. D.: The Shelf Operation in the Treatment of Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17**, 43.

[15] Doran, W. G.: Early Symptoms of Congenital Dislocation of the Hip Joint. Jour. Med. Soc. N. J., **29**, 564.

[16] Faber, Alex.: Zur Prognose der Unblutig Reponierten Angeborenen Hüftluxation. Ztschr. f. Orth. Chir., **62**, 359.

[17] Farrell, B. P., and Howorth, M. B.: Open Reduction in Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17**, 35.

[18] Freiberg, A. H.: Congenital Luxation of the Hip. Jour. Bone and Joint Surg., **17**, 1.

[19] Gaenslen, F. J.: Schanz Subtrochanteric Osteotomy for Irreducible Dislocation. Jour. Bone and Joint Surg., **17**, 16.

[20] Gaugele-Kienzle: Die Erfolge bei der Behandlung der Sogenannten Angeborenen Hüftgelenksverrenkung. Deutsch. Ztschr. f. Chir., **245**, 214.

[21] Gichler, H.: Ein Beitrag zur Frage der Luxatio Coxae Congenita. Arch. f. Orth. u. Unfall Chir., **33**, 248.

[22] Gill, A. B.: Operation for Old or Irreducible Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **10**, 696.

[23] Gill, A. B.: Plastic Construction of the Acetabulum in Congenital Dislocation of the Hip. The Shelf Operation. Jour. Bone and Joint Surg., **17**, 48.

[24] Herbst: Die Blutige Einrenkung der Angeborenen Hüftgelenkluxation. Deutsch. Ztschr. f. Chir., **217**, 359.

[25] Howorth, M. B., and Smith, H. W.: Congenital Dislocation of the Hip Treated by Open Operation. Jour. Bone and Joint Surg., **14**, 299.

[26] Howorth, M. B.: Shelf Stabilization of the Hip. Jour. Bone and Joint Surg., **17**, 945.

[27] Kidner, F. C.: Comparative Analysis of the Results of Open and Closed Reductions in Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **17**, 25.

[28] Lowendorf, C. S.: The Bifurcation Operation. Jour. Bone and Joint Surg., **15**, 493.

[29] Ober, F. R.: Shelf Operation to Relieve Persistent Dislocation of the Hip. Jour. Bone and Joint Surg., **17**, 73.

[30] Øwre, Axel: Painful Congenital Subluxation of the Hip. Acta Chir. Scand., **76**, 369.

[31] Putti, V.: The Early Treatment of Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **15**, 16.

[32] Schede, F.: Zur Frage der Ergebnisse der Reponierten Hüftluxation. Arch. f. Orth. Chir., **60**, 474.

[33] Steindler, A., Kulowski, J., and Freund, E.: Congenital Dislocation of the Hip. J.A.M.A., **104**, 302.

[34] Swett, P. P.: An Operation for the Reduction of Certain Types of Congenital Dislocation of the Hip. Jour. Bone and Joint Surg., **10**, 675.

[35] Tillmans, W.: Die Kongenitalen Hüftluxationen. Deren Behandlung und Ergebnisse. Ztschr. f. Orth. Chir., **53**, 52.

(*To be continued*)

THE TOXIN OF BURNS

SOL ROY ROSENTHAL, M.D., Ph.D.

CHICAGO, ILL.

FROM THE DEPARTMENTS OF THERAPEUTICS AND BACTERIOLOGY OF THE UNIVERSITY OF ILLINOIS COLLEGE OF MEDICINE, CHICAGO, ILL.

THE theories explaining the toxic manifestations following extensive burns are (Harkins[4]):

(1) *Physical,* in which there is a local leakage of plasma into the tissues altering the circulation and resulting in a diminished blood volume, a diminished cardiac output, and finally a collapse of the blood pressure (the diminished blood volume is accompanied by an increased concentration of blood and hemoglobin).

(2) *Toxic,* whereby the supposed toxemia caused by the burn results, after a certain time, in shock and death.

Whereas the earlier authors (Parascandolo,[12] Pfeiffer,[14] Lewis and Grant[9]) demonstrated the presence of a toxic substance in the blood of burned individuals (later Robertson and Boyd,[15] Shimada,[17] Nagamitu[10]), the more recent authors question the presence of a toxin (Harrison and Blalock,[7] Harkins,[5] Wilson and Stewart, Underhill and Kapsinow[18]). Indeed, Underhill and Kapsinow emphasized that as long as we entertain the idea of a burn toxin, the progress in the understanding of burns and its therapy will be delayed.

One of the important factors in the modern concept of the pathogenesis in burns (and traumatic shock) is that there is a local accumulation of fluid which begins immediately or shortly after the injury, and continues thereafter, resulting in a decrease of the blood volume and an increase in the blood concentration. According to Harkins and others, if the process is too severe, the cardiac output decreases, and when this reaches one-third its normal, the blood pressure falls and death ensues as a result of cardiac failure—secondary shock (Underhill, Kapsinow and Fisk, Blalock, Harkins for burns; and Roome, Keith and Phemister,[16] Parsons and Phemister[13] for traumatic shock).

The protagonists of the toxic theory have offered many possibilities as to the nature of this toxin. Parascandolo links it to the ptomaines. Pfeiffer believes it resembles the nucleoproteins of snake venom. Robertson and Boyd believe it to be primary and secondary proteoses. The latest concept is that it is histamine-like in character because it effects a drop in blood pressure (rabbits and cats), and it contracts smooth muscle (uterus, intestinal strip—Shimada, Nagamitu).

The following experiments were undertaken to determine whether or not

Submitted for publication December 23, 1936.

histamine-like substances were present in the blood of burned animals or humans.

METHOD.—Blood was drawn from burned (anesthetized) shoats (size of burn = 100 to 250 square inches), adult pigs (size of burn = 100 to 550 square inches), and guinea-pigs (size of burn = 4.8 to 9.6 square inches) at regular intervals in the course of the experiment. The tail method for obtaining blood was used for the shoats and adult pigs. Blood from humans (adults and children) was obtained at varying intervals after burns (three days to 13 months). In one case of traumatic shock, blood was obtained two hours after injury.

Serum, red blood cells, citrated blood, and hemolized blood were examined for their ability to contract a virgin guinea-pigs' (200 to 300 Gm.) uterus (method of Dale and Laidlaw[1]). The uterus-ovary preparations were suspended by means of glass hooks to a suitable lever and immersed in 35 cc. of Ringer-Locke's solution (aerated). The lever was approximated to a kimograph, and the oscillations of the lever recorded. The removal of fluid or addition of same into the preparation was accomplished by suction and delivery applied to the bottom of the tube. In this way the muscle preparation was never molested and suffered minimal extraneous irritations. The Ringer-Locke containing tube was immersed in a constant water bath (37° C.), and all solutions added to the fluid were first warmed to the same temperature. After suspending the uterus-ovary preparation, about 15 to 20 minutes were allowed for relaxation of the muscle. The latter being attained, the next step in all instances was to add 1 cc. of a 1:100,000 histamine solution, made up in Ringer-Locke's. (This amount gave the most satisfactory contraction to the uterus as indicated by the lever rise.) The height of the elevation produced by histamine was used as a basis of comparison. After each procedure the specimen was washed three times, using from 100 to 150 cc. of Ringer-Locke solution. Relaxation to the original base line was effected before another testing solution was added (15 to 30 minutes). At the end of each experiment, the action of histamine was again determined.

Sterile blood specimens were collected and kept in the ice-box until used. Every specimen (except those used immediately after bleeding) was treated with phenol (0.5 per cent), or a few drops of chloroform added (three drops to 20 cc.) to prevent bacterial activity.

RESULTS.—*(I) Normals:* The serum, citrated blood, washed red blood corpuscles, or hemolyzed serum obtained from normal shoats, adult pigs (Fig. 1), guinea-pigs and humans did not contract the virgin guinea-pigs' uterus as noted by the kimograph tracings. Examinations were made from one to 24 hours after withdrawal of blood.

(II) Burned Cases.—Shoats: As a rule, smooth muscle contracting substances were detected in the blood of burned shoats one hour after the beginning of the experiment (Fig. 2). At this time only the citrated blood and the R.B.C. contained the active principle. From 18 to 24 hours later this substance was found mainly in the serum (Fig. 3). Traces of an histaminoid

substance were at times noted in the R.B.C. up to two weeks, but this was not the rule. From 20 to 28 days this substance could not be detected by the above method (Table I). (The wounds by this time had healed under a scab without infection.)

Adult Pigs.—After apparent healing of the burned sites (one month after the onset of the experiment), large slices of scarred areas, including skin and subcutaneous fat, were removed for microscopic section. Because of the

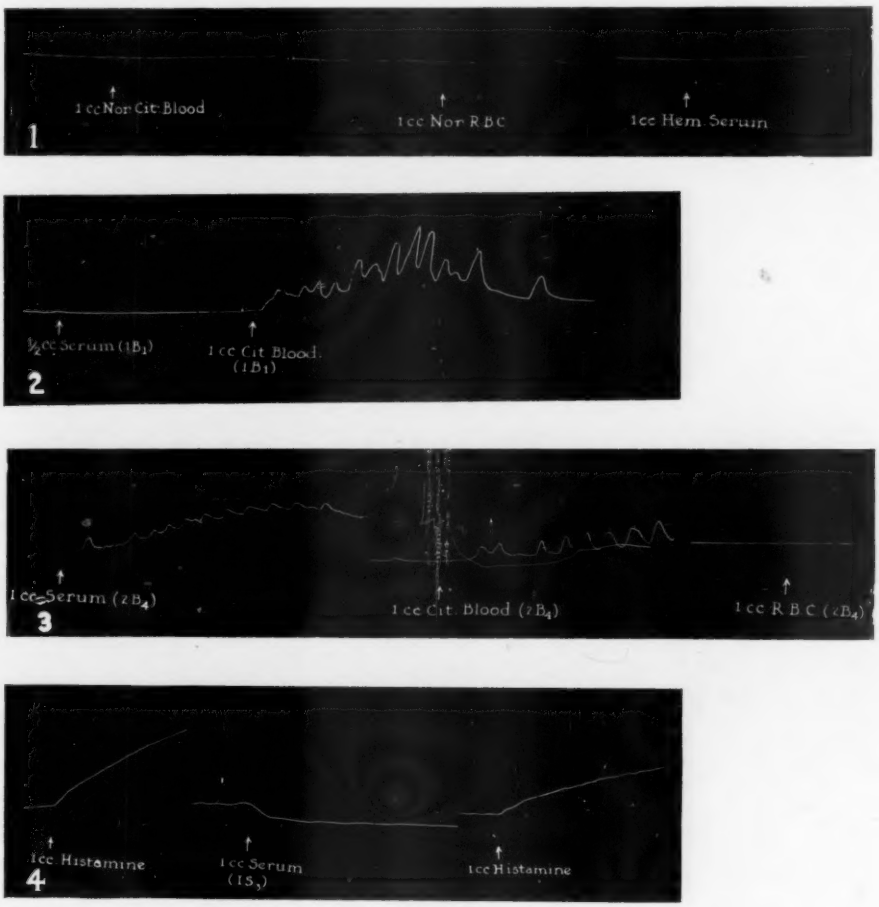


FIG. 1.—The action of normal blood on the virgin guinea-pig uterus.
FIG. 2.—The action of burned shoat blood (1 hr.) on the virgin guinea-pig uterus.
FIG. 3.—The action of burned shoat blood (19 hrs.) on the virgin guinea-pig uterus.
FIG. 4.—The action of burned shoat blood (3 da.) on the virgin guinea-pig uterus.

numerous burn sites, approximately 15 to 25 square inches were removed from each pig. These wounds were slow in healing. Two of three pigs thus treated contained in their serum smooth muscle contracting substances five months after the last burn and two months after the removal of the biopsies. The wounds had superficially healed in all cases when blood was first withdrawn, but it was difficult to decide whether or not the processes

of healing and absorption were still going on beneath the superficial approximation.

TABLE I

THE PRESENCE OF AN HISTAMINOID SUBSTANCE IN THE BLOOD OF BURNED SHOATS

Time after Burn	Action on Virgin G. P. Uterus			Time after Burn	Action on Virgin G. P. Uterus		
	S.	cit. b.	R.B.C.		S.	cit. b.	R.B.C.
0.....	0	0	0	0.....	0	0	0
1 hr.....	0	++	—	2 hrs....	0	++	+
18 hrs.....	0	++	—	19 hrs....	+++	tr.	0
27 hrs.....	+++	+	—	45 hrs....	0	0	0
44 hrs.....	+++	+	—	3½ da...	++	++	0
5 da.....	+++	tr.	++	8 da.....	++	+	0
2 wks....	++	+	—	20 da.....	0	0	0
28 da.....	0	0	0				
40 da.....	0	—	—				

++ = action of 1 cc. of a 1:100,000 histamine solution; S = serum; cit. b. = citrated blood; R.B.C. = red blood corpuscles; tr. = trace; the negative sign (—) indicates test not performed.

TABLE II

THE PRESENCE OF AN HISTAMINOID SUBSTANCE IN THE BLOOD OF BURNED GUINEA-PIGS

No.	Size of Burn (sq. in.)	1 hour	5 days	25 days
13	8.40	0 (cit. b.) tr. (R.B.C.)	+ (S.) +++ (R.B.C.)	
371	7.04	+ (cit. b.)	++ (R.B.C.) tr. (S.)	
321	8.40	0 (cit. b.)	tr. (S.)	0 (S.)
19	8.32	0 (cit. b.) tr. (R.B.C.)	+ (R.B.C.)	0 (S.)
265	8.96	0 (cit. b.) tr. (R.B.C.)		
23	7.84		0 (S.) ++ (R.B.C.)	
330	7.68	++ (cit. b.)	++ (R.B.C.)	
235	8.16	tr. (S.) ++ (R.B.C.)		
82	8.96	+ (R.B.C.)		
227	4.80	+ (cit. b.)		
25	7.36	++ (cit. b.)		
234	4.80		+ (R.B.C.)	0 (S.)
338	8.32		++ (R.B.C.)	
333	9.60	0 (cit. b.) tr. (R.B.C.)	0 (S.)	0 (S.)

++ = action of 1 cc. of a 1:100,000 histamine solutions; S. = serum; cit. b. = citrated blood; R.B.C. = red blood corpuscles; tr. = trace.

Guinea-Pigs.—One hour after the beginning of the experiment, an histaminoid substance was demonstrable in the R.B.C. After five days the serum, too, contained this element, but not to the extent of that found in the R.B.C. After 25 days the specimens examined (serums) were devoid of active principles.

Humans.—Table III summarizes the effect of the blood on the guinea-pigs' uterus. An histaminoid substance was not detected until five days following a burn. With healing, these bodies were found only in traces by the third to fourth week, whereas if the wound was more extensive and healing slow (usually associated with a slight infection) this substance persisted for a longer period of time.

TABLE III

THE PRESENCE OF AN HISTAMINOID SUBSTANCE IN THE BLOOD OF BURNED HUMANS

Name	Age—Sex	Time after Burn	Action on Guinea-Pigs' Uterus	Size and Condition of Burn
F. Z.	46—M.	—	o (S.)	Normal
R. T.	31—M.	3 da.	o (S.)	Chest and left arm—2nd degree
H. J.	65—M.	5 da.	tr. (S.)	Both hands—2nd degree
N. K.	39—F.	19 da.	+ (S.)	Both legs—2nd and 3rd degrees
C. I.	35—M.	22 da.	tr. (S.)	Arm and back—2nd degree. Slight infection; healing rapid
S. P.	36—M.	25 da.	tr. (S.)	Legs and arms—2nd degree. Slight infection; healing rapid
D. D.	21—M.	27 da.	++ (S.)	Legs—2nd degree. Slight infection; low grade temperature
P. G.	65—M.	34 da.	+++ (S.)	Arms and legs—2nd degree. Wounds clean; healing
R. C.	8—F.	37 da.	+ (S.)	Neck, abdomen and thigh—2nd degree. Slight infection, slight temperature
M. M.	9—F.	68 da.	+ (S.)	Right chest and arm—2nd degree. Slight infection, but healing
C. P.	40—M.	13 mos.	tr. (S.)	Keloids of abdomen and thigh. Recently healed graft
E. S.	15—M.	2 hrs.	+ (S.)	Shock due to multiple fractures

++ = action of 1 cc. of a 1:100,000 histamine solution; S. = serum; R.B.C. = red blood corpuscles; tr. = trace; F. = female; M. = male.

DISCUSSION.—As the experimental data indicate, there appears in the blood of burned animals (shoats, pigs and guinea-pigs) and humans a substance which causes contraction of the guinea-pigs' uterus.

This substance was first linked with the R.B.C., and after 18 to 24 hours was found in the serum (shoats). In guinea-pigs the R.B.C. were found to contain an histaminoid substance up to five days. In humans an histaminoid substance was not present until five days after the burn. In one case of

shock, examined early, this substance was detected. Normal serums of animals or humans examined fresh or after one to 14 days did not contain histaminoid substances.

The intraperitoneal injection of 2 cc. of burned swine serum into guinea-pigs was without noticeable effect. However, burned guinea-pigs injected with this same serum subcutaneously undermining the wound or intraperitoneally (unheated or heated at 60° C. for half an hour) resulted in the death of four out of six guinea-pigs. On the other hand, burned guinea-pigs treated similarly with saline (eight pigs) and normal serum (four pigs) remained immune. Postmortem examination of the guinea-pigs revealed a marked dehydration and hyperemia of the internal organs with a slight ecchymosis. The lungs were not distended.

The ability of this burn toxin to contract the virgin guinea-pigs' uterus would naturally associate it with histamine, for the latter substance has the same properties. Yet points of divergence were noted. When the blood of pigs containing this histaminoid substance was heated for half an hour at 60° C., it lost its ability to contract the guinea-pigs' uterus. Histamine so treated retained this potency (150° to 170° C. decreases the action of histamine according to Feldberg and Schilf[3]). Furthermore, upon several occasions after adding the burn toxin to the muscle preparation, a contraction as usual resulted, but after washing and again adding the same serum a demonstrable contraction failed to appear. Histamine in such instances caused a definite contraction if added immediately after the above or after washing (Fig. 4).

Comment.—Histamine-like substances are supposedly present in the normal blood but in an inactive form (Feldberg and Schilf). Histamine, if injected slowly, in many times its lethal dose, cannot be detected in the blood of rabbits (Oehme,[11] von Guggenheim and Loeffler[19]). Supposedly the lung and the liver remove this substance very rapidly from the blood stream. Some animals are more susceptible to histamine than others, the mechanism not being understood. The differences in animal susceptibility may account for the variations in the amount of histaminoid substance in the blood of the pig and in the human following burns. Why the 45 hours blood specimen of the shoat studied did not contract the guinea-pigs' uterus and the three and one-half day specimen did, cannot be explained.

Lewis and Grant[9] described an histamine-like substance ("H" substance) as a normal product of the skin, and upon irritation of the latter large quantities of the former may be liberated. Harris[6] has isolated as much as 10 mg. of histamine per kilogram of human skin. Most authors are agreed that histamine causes an increased permeability of the capillaries resulting in an exudation of plasma and retardation of the blood flow through the capillaries (Dale and Laidlaw, Feldberg and Schilf). In sufficient quantities histamine causes a decrease in blood volume and an increase in hemoglobin concentration as a result of the above mechanism (Dale and Laidlaw, Eppinger and Schürmeyer,[2] Lamson, Abt, Oosthuisen and Rosenthal[8]). This

action, as has already been stated, is precisely what occurs following burns, according to the protagonists of the physical theory.

SUMMARY.—In the blood of burned shoats, adult pigs, guinea-pigs and humans, a substance was found that caused contraction of the virgin guinea-pigs' uterus. This substance was at first linked with the red blood corpuscles, but was later found in the serum. The above differs from histamine in that it is heat labile and it does not act upon the virgin guinea-pigs' uterus under certain conditions when histamine does.

It was noted that the local action of histamine is similar in many respects to the local pathology in burns and shock.

I wish to thank Dr. Bernard Fantus and Dr. Lloyd Arnold for their interest in this work.

REFERENCES

[1] Dale, H. H., and Laidlaw, P. P.: J. Physiol., **41**, 318, 1910–1911; **52**, 110, 1918.
[2] Eppinger, H., and Schürmeyer, A.: Klin Wchnschr., **7**, 777, 1928.
[3] Feldberg, W., and Schilf, E.: Histamin. Julius Springer, Berlin, 1930.
[4] Harkins, N. H.: ANNALS OF SURGERY, **102**, 444, 1935; Arch. Surg., **31**, 71, 1935.
[5] Harkins, N. H., Wilson, W. C., and Stewart, C. P.: Proc. Soc. Exper. Biol. & Med., **32**, 913, 1935.
[6] Harris, K. E.: Heart, **14**, 161, 1927.
[7] Harrison, W. G., Jr., and Blalock, A.: ANNALS OF SURGERY, **96**, 31, 1932.
[8] Lamson, P. D., Abt, A. F., Oosthuisen, C. A., and Rosenthal, S. R.: J. Pharmacol. & Exper. Therap., **21**, 401, 1923.
[9] Lewis, T. H., and Grant, R. T.: Heart, **11**, 210, 1924.
[10] Nagamitu, G.: Jap. J. M. Sc., **3**, 81, 1934.
[11] Oehme, C.: Arch. f. exper. Path. u. Pharmakol., **72**, 76, 1913.
[12] Parascandolo, K.: Wien. med. Wchnschr., **54**, 575, 620, 676, 1904.
[13] Parsons, E., and Phemister, D. B.: Surg., Gynec. & Obstet., **51**, 196, 1930.
[14] Pfeiffer, H.: Münchem. med. Wchnschr., **61**, 1099, 1329, 1914.
[15] Robertson, B., and Boyd, B. S.: J. Lab. & Clin. Med., **9**, 1, 1923.
[16] Roome, N. W., Keith, W. S., and Phemister, D. B.: Surg., Gynec. & Obstet., **56**, 161, 1933.
[17] Shimada, T.: Jap. J. M. Sc., **4**, 26, 1934.
[18] Underhill, F. P., Kapsinow, R., and Fisk, M. E.: Am. J. Physiol., **95**, 302, 1930.
[19] Von Guggenheim, M., and Loeffler, W.: Biochem. J., **72**, 325, 1916.

SPINAL ANESTHESIA*

A STUDY OF THE POSTOPERATIVE COURSE

EDWIN P. LEHMAN, M.D., AND JOHN C. RISHER, M.D.
UNIVERSITY, VA.,
AND
WILLIAM E. BIPPUS, M.D.,
WHEELING, W. VA.

FROM THE DEPARTMENT OF SURGERY AND GYNECOLOGY, UNIVERSITY HOSPITAL, UNIVERSITY OF VIRGINIA SCHOOL OF MEDICINE, UNIVERSITY, VA.

THE importance of determining by statistical study, rather than by clinical impressions, the place of any method of anesthesia needs no emphasis. Attempts to obtain numerical data are usually limited to the determination of operative mortality rates and the percentage incidence of postoperative complications. The surgeon's ease at the operating table, particularly when muscular relaxation is needed, and the smoothness of the uncomplicated postoperative course are usually matters of clinical impression. In the case of spinal anesthesia, the clinical judgment is often expressed that operative difficulties are minimized, and that the postoperative course is smoother than with inhalation anesthesia. Although the mortality rate and the incidence of complications will be presented, the present study places emphasis on statistical data from the postoperative course in an attempt to substitute accurate figures for clinical impressions.

Contraindications.—In the Departments of Surgery and Gynecology, and of Urology and Proctology in the University of Virginia Hospital, spinal anesthesia has been used, since 1929, as a routine in all cases requiring operations below the diaphragm, unless contraindications are present. The contraindications recognized by the Department of Surgery and Gynecology may be divided into two groups. The first includes cases that are primarily unsuitable for spinal anesthesia, such as those in which local or peripheral block anesthesia is possible, those in which minor quick procedures are contemplated (dilatation and curettage, incision and drainage, colpotomy, onychiectomy, *etc.*) and those in which such procedures as laminectomy or an operation for spina bifida are planned. The second group consists of cases primarily suitable for spinal anesthesia in which other factors contraindicate its use. In this group may be listed: (1) Infancy, with a tendency to infrequent use in young children; (2) arterial hypotension, especially as the result of shock; (3) the very ill patient, particularly from peritonitis or intestinal obstruction; (4) the patient with obviously unstable emotional balance; (5) an occasional patient to whom choice of anesthesia is allowed for psychologic reasons; and (6) local factors, including septic processes in the tissues of the back, and severe osteo-arthritis of the spine in which spinal anesthesia is either not at-

* Read before the Southern Surgical Association, Edgewater Park, Miss., December 16, 1936.

tempted or fails through failure to enter the canal. Although warning is often given against the use of spinal anesthesia in arterial hypertension, we have not considered an elevated blood pressure a contraindication. In cases presenting the possibility of coronary disease, particular pains are taken to prevent a fall in blood pressure on account of the danger of coronary thrombosis. In all cases of hypertension, in fact, the attempt is made to maintain the blood pressure at its original level.

Material.—While the technic of spinal anesthesia was being learned in this clinic, there were a small number of deaths that could probably be ascribed to the method. The mortality figures to be presented do not cover this early period; they are limited to a later five year period, 1931–1935 inclusive, in which the technic had been largely standardized. During this period 13,761 anesthesias were administered in the operating room, exclusive of those administered for tonsillectomy. Of these, 3,539 were spinal anesthesias, an average incidence of 25.7 per cent (Table I). The yearly incidence of the use of spinal anesthesia shows regularly diminishing employment in spite of

TABLE I

ANESTHETICS ADMINISTERED IN OPERATING ROOM (1931–1935 INCLUSIVE)*
(*Tonsillectomies and Adenoidectomies Excluded*)

Year	Number of Operations	Operations under Spinal Anesthesia	Per Cent
1931	2,083	654	31.4%
1932	2,187	718	32.8%
1933	3,179	835	26.2%
1934	3,297	705	21.4%
1935	3,015	627	20.8%
Totals	13,761	3,539	25.7%

* The diminishing incidence of use shown in this table must be interpreted in the light of Table II and the comment in the text.

TABLE II

PERCENTAGE INCIDENCE OF EMPLOYMENT OF SPINAL ANESTHESIA BY THE DEPARTMENT OF SURGERY AND GYNECOLOGY FOR THE YEAR 1935

Total operations			1,433
Spinal anesthetics			577
General incidence of spinal anesthetics			38.8%
Total operations below the diaphragm			898
Local anesthetics		52	
D. & C. and radium application	(General anesthesia)	118	
Incision and drainage, *etc.*	(General anesthesia)	92	
Laminectomy and spina bifida	(General anesthesia)	8	
Total cases primarily unsuitable for spinal anesthesia			270
Cases primarily suitable for spinal anesthesia			628
Spinal anesthetics			557
Incidence of spinal anesthetics in primarily suitable cases			88.7%

general clinical satisfaction in the services on which it is routine, a decline believed to represent largely a diminishing use on other services. This is indicated by the incidence of use in the Department of Surgery and Gynecology for the single year 1935 (Table II). This service has in that period employed spinal anesthesia in 88.7 per cent of cases which were primarily suitable for its use. The remaining 11.3 per cent, in which general anesthesia was employed, represents cases in which true contraindications to spinal anesthesia were recognized.

This study presents: (1) A consideration of the operative mortality in the five year series of 3,539 cases; (2) a comparative study of the postoperative course in 900 selected cases, 450 under general anesthesia and 450 under spinal anesthesia; and (3) a comparison of the postoperative complications in the same group of 900 cases.

Technic.—The following description presents the method now employed in this hospital in inducing spinal anesthesia. It is, of course, in no point original, having been developed from standard methods.

Preoperative preparation in elective cases includes, ordinarily, no intake of food or fluid after midnight. In most upper abdominal cases and in cases in which prolonged operations are expected, intravenous infusions of normal salt solution or glucose are given before the patient is brought to the operating room. About 20 minutes before the administration of the spinal anesthetic, morphine sulphate Gr. 1/6, hyoscine hydrobromide Gr. 1/150, and ephedrine sulphate Gr. ¾ are given hypodermically. As a result of the morphine and hyoscine, the patient's mental and emotional activities are depressed often to a degree permitting sleep during the operation.

The patient is placed on his side on the operating table and the back surgically cleaned. After infiltration of the skin and subcutaneous tissues with 0.5 per cent procaine, the lumbar puncture needle (No. 18 to No. 22) is inserted, using the midline route. For operations on the lower abdomen and extremities, the space below the first or second lumbar vertebra is usually chosen; for operations in the upper abdomen, the space below the twelfth thoracic vertebra. The puncture is not considered satisfactory unless cerebrospinal fluid can be freely withdrawn by syringe suction.

After experience with various drugs, including spinocaine, pantocain, and neocaine, the routine drug now employed is procaine (Squibb) in crystalline form. The usual dose varies from 150 mg. for the average adult to 50 mg. for a young child; in upper abdominal cases in large individuals 200 mg. may be employed. For operations on the kidney, the urologic department still employs spinocaine. The desired amount of procaine is dissolved in from 1 to 2 cc. of the patient's spinal fluid which is then reinjected without barbotage.

The patient is then immediately placed on his back with the head of the table lowered about ten degrees, and blood pressure readings are begun. If the blood pressure tends to drop, ephedrine sulphate Gr. ½ or adrenalin minims three are given, either of which may be repeated. In the occasional case, when these measures are insufficient, an intravenous infusion follows. In a prolonged operation when restlessness begins, indicating the impending termination of the analgesia, anesthesia is immediately instituted by inhalation of nitrous oxide and oxygen, and, if necessary, full ether anesthesia may follow. For nausea and an occasionally observed fear-state focused on the

respiration, oxygen inhalations are employed. At the close of the operation the usual mixture of carbon dioxide and oxygen is given for about 15 breaths. If a successful puncture is effected, as indicated by a free flow of fluid, satisfactory anesthesia is obtained in over 95 per cent of instances. In an occasional case a previously unsuccessful injection has been immediately repeated, without unfavorable symptoms and with a satisfactory anesthetic result.

With the present technic, disturbing physiologic phenomena have been unusual. In about half the cases there has been no significant drop in blood pressure. Most of the remaining cases have shown a transient drop in blood pressure to a level of 90 to 100 Mm. of mercury, which disappears promptly following the exhibition of pressor drugs. Even an occasional greater drop in the blood pressure almost invariably responds to treatment unless loss of blood and the surgical manipulation superimpose secondary shock upon the drug action.

The methods of general anesthesia employed in the cases reported herein include only inhalation of nitrous oxide and oxygen, alone, or combined with ether.

Mortality.—The determination of operative mortality is of course the first approach to the determination of the propriety of any anesthetic. The difficulties of relating death at, or following, operation to the anesthetic administered are obvious. It is difficult to determine that death during an operation in a desperate case occurred on account of the anesthetic, and not on account of the disease or the operative manipulations, a difficulty intensified by poor surgical judgment and unskillful surgical technic. Furthermore, the place of the anesthetic in determining later death is even more difficult to determine. Whether coronary thrombosis, or peripheral thrombosis with death from pulmonary embolism, or a fatal pneumonia resulted from the choice of anesthesia, is practically never determinable. These considerations make the formulation of mortality rates a somewhat uncertain venture.

In the present study, deaths in the five year group (3,539 cases) have been listed in two categories: (1) Deaths occurring on the operating table; and (2) deaths occurring within 24 hours of operation. It is assumed that later deaths cannot be ascribed to the anesthesia. The hospital histories of the cases in both of these groups have been studied in detail.

It must be noted that the number of spinal anesthesias administered is somewhat greater than the number of patients treated, as a small proportion of the latter were given more than one spinal anesthetic. The mortality rate is based on the number of anesthetics given, and not on the number of patients treated. All successful administrations of spinal anesthesia are included, whether or not a general anesthetic had to be administered later during the course of the operation.

In the 3,539 cases there were three fatalities on the operating table, the pertinent clinical facts of which follow:

Data Relevant to Fatalities during Operation

Case 1.—Operation for an enormous inguinal hernia, strangulated for four days, in a man of 82, who was uremic and moribund. The surgeon's notes stated that the

hernia was too large for local infiltration. It is probable that questionable surgical judgment was used in undertaking operation upon this patient. Death is obviously not to be ascribed to the anesthetic.

Case 2.—Operation for a gunshot wound of the abdomen with massive intra-abdominal bleeding. Operation was undertaken with the patient in shock, and death occurred from uncontrollable hemorrhage. If bleeding had been controlled and the patient had died, the influence of the spinal anesthetic in the fatality might well be raised.

Case 3.—Operation for gunshot wound of the abdomen and chest in a colored male of 24, performed in 1933 by the surgical resident. The patient was admitted one hour after being shot with a .32 caliber pistol and presented three bullet wounds in the chest and abdomen. There was evidence of fluid in the left chest on physical and roentgenologic examination. Abdominal examination showed tenderness in the left flank, normal liver dulness, and very little muscle spasm. The patient's general condition was excellent, pulse 120, blood pressure 180/80. The urine was negative, and the leukocyte count 5,000. There was some uncertainty as to whether there had been intra-abdominal injury, and exploration was properly undertaken. The usual dose of ephedrine Gr. ¾ was not given in this instance as a preliminary preparation. Neocaine, 200 mg., was injected in the lumbar region dissolved in 3 cc. of spinal fluid. Ephedrine Gr. ¾ was administered as soon as the lumbar puncture needle was withdrawn. There was rather prompt anesthesia, beginning in the feet, which at the time of incision had reached the costal margin. Exploration revealed about 200 cc. of free blood in the peritoneal cavity, apparently coming from a furrow which had been plowed in the surface of the spleen by a bullet found lying free in the peritoneal cavity. A penetrating wound in the diaphragm at the eleventh intercostal space was also found. During the exploration the anesthesia progressed rapidly to the shoulders and the blood pressure fell progressively in spite of the administration of ephedrine Gr. 1, adrenalin minims 5, and caffeine Gr. 7½. Before the exploration was complete, respiration ceased and the pulse began to fail. Artificial respiration was instituted, together with cardiac massage given through the diaphragm and the administration of adrenalin minims 10 into the heart muscle. None of these measures checked the patient's rapid failure. Death occurred 45 minutes after administration of spinal anesthesia.

Postmortem examination revealed about 300 cc. of bloody fluid in the peritoneal cavity and about 300 cc. of fresh blood in the pleural cavity. There were no fatal visceral injuries disclosed. Although the cord and brain were not examined, the pathologist expressed the opinion that the injuries were not sufficient to cause death. This case has therefore been unequivocally ascribed to spinal anesthesia. Variations from the present technic must be emphasized in this case, chiefly in the omission of preanesthetic ephedrine, and in the employment of 3 cc. of spinal fluid for solution of the drug.

Twelve additional patients died within 24 hours after operation. Of these deaths, seven were so obviously the result of the disease rather than the operation that they will not be presented separately. The remaining five deaths were definitely associated with the operative procedures. The cases may be briefly presented as follows:

Data Relevant to Five Cases that Died within 24 Hours Postoperatively

Case 1.—Exploration for retroperitoneal sarcoma. In this case the surgical procedure was obviously carried too far in attempting a radical cure.

Case 2.—Attempted resection of an inoperable carcinoma of the ascending colon in a man of 65. The same comment can be made here as in Case 1.

Case 3.—Exploration in a case of generalized peritonitis in an extremely ill patient. In this case it is probable that any surgical procedure was ill-advised.

Case 4.—Operation for an extra-uterine pregnancy of seven months' duration, located within the broad ligament. The operation was difficult and prolonged, the patient dying from gradually developing surgical shock.

Case 5.—Amputation of the thigh for chronic osteitis of the tibia following a compound fracture suffered one month previously by a diabetic patient of 60. The patient left the table in shock. An unnecessarily prolonged operation in an ill patient whose diabetes was improperly controlled prevents the conclusion that death was due to the anesthetic.

An analysis of these 15 fatalities indicates that only one death was definitely due to spinal anesthesia; a mortality rate in 3,539 spinal anesthesias of 0.028 per cent.

Postoperative Course.—In an attempt to minimize the variable factors always present in clinical comparisons, the postoperative course following spinal anesthesia and general anesthesia was studied in three groups of elective surgical procedures for diseases which in themselves affect the operative prognosis to a minimal degree, namely: (1) Operations for nonstrangulated inguinal hernia (400 cases); (2) perineorrhaphy (253 cases); and (3) hysterectomy for fibromyoma and prolapsus uteri (247 cases). In this group no panhysterectomies are included, nor are hysterectomies in the presence of pelvic infections, pregnancy, or malignant disease. Selection included rejection for inadequate records. Cases complicated by serious unrelated diseases, such as tuberculosis and cardiac lesions, and by additional surgical procedures were also rejected.

Half of the 900 operations were performed under spinal anesthesia and half under inhalation anesthesia. It happens that the time at which spinal anesthesia began to be freely used corresponds roughly to the time at which stress was laid upon adequate postoperative notes in the Department of Surgery and Gynecology. Certain data therefore tend to be available in more detail in the spinal anesthesia group than in the general anesthesia group. For this reason certain of the tables to be presented do not include the entire group of cases studied. If, for example, the data are available for 192 cases of herniorrhaphy under general anesthesia, the first 192 cases of herniorrhaphy under spinal anesthesia are used in comparison. The material presented in studying the postoperative course is not limited to the five year period on which mortality figures are based, but is taken at random from the files in the record room.

Average Highest Postoperative Pulse Rate, Temperature and Respiratory Rate.—Table III shows the comparisons under spinal anesthesia and under inhalation anesthesia of the average highest postoperative pulse rate, temperature, and respiratory rate. A possible error is introduced in comparing the postoperative temperatures, in that no attempt has been made to separate readings by mouth from those by rectum. During the last few years, which correspond to the period of routine use of spinal anesthesia, the nurses have been instructed to take all readings for three days after operation by rectum.

During an earlier period this routine did not exist, a period from which the majority of cases under inhalation anesthesia are taken. If all readings were reduced to mouth values, therefore, it is probable that the average highest postoperative temperature after spinal anesthesia would be almost a degree lower than that actually obtained. The comparisons show a slight differential in favor of spinal anesthesia in postoperative pulse rate, temperature and respiratory rate in each group of cases, and in all groups combined.

TABLE III

AVERAGE MAXIMUM POSTOPERATIVE PULSE RATE, TEMPERATURE AND RESPIRATORY RATE*

	GENERAL				SPINAL			
	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined
No. of cases	200	148	102	450	200	105	145	450
Pulse rate	103.3	101.2	108.2	103.7	95.9	100.4	106.2	100.0
Temperature	101.2	100.4	101.4	101.0	101.1	100.3	101.0	100.8
Respiratory rate		22.4	23.7	22.7†		21.6	23.0	22.4†

* The figures shown in this table were obtained by adding the highest recorded figure on each bedside chart and dividing by the number of cases.

† 250 cases only.

Nausea, Vomiting, Distention, Headache and Backache.—Table IV shows the incidence of nausea, vomiting, distention, headache and backache. The conclusions to be drawn from the study of these factors must be tentative because of the uneven thoroughness of the postoperative notes. The percentages of the combined series are uniformly slightly in favor of spinal anesthesia. The only striking discrepancy is a greater frequency of distention in the hernia cases performed under spinal anesthesia compared to those performed under general anesthesia. This is compensated for by a greater incidence of distention under general anesthesia in the cases of hysterectomy. An interesting

TABLE IV

PERCENTAGE INCIDENCE OF POSTOPERATIVE NAUSEA, VOMITING, DISTENTION, HEADACHE AND BACKACHE*

	GENERAL				SPINAL			
	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined
Nausea	18.2% (187)	27.7% (148)	21.5% (102)	22.2% (437)	18.7% (187)	16.1% (105)	21.3% (145)	19.0% (437)
Vomiting	10.7% (187)	19.6% (148)	35.3% (102)	19.4% (437)	10.7% (187)	19.0% (105)	28.8% (145)	18.7% (437)
Distention	8.1% (160)	27.7% (148)	69.0% (102)	30.2% (410)	16.3% (160)	20.0% (105)	30.3% (145)	22.2% (410)
Headache	8.1% (186)	9.5% (148)	13.8% (102)	9.8% (436)	7.5% (186)	6.6% (105)	6.9% (145)	7.1% (436)
Backache	7.5% (186)			7.5% (186)	4.3% (186)			4.3% (186)

* The figures presented in parentheses represent the number of cases studied in each instance to obtain the percentages given.

observation deserves emphasis, namely, that both headache and backache are more frequently recorded in cases operated upon under general anesthesia than in those under spinal anesthesia.

Urinary Retention.—An attempt to measure the incidence and persistence of urinary retention under the two types of anesthesia is seen in Table V, where are recorded the number of cases catheterized, and the number catheterized more than twice. It is seen in each group that spinal anesthesia shows slightly fewer postoperative catheterizations than does general anesthesia. Inasmuch as it is an intern habit to record catheterization, it is believed that these figures tend to be accurate.

TABLE V

PERCENTAGE INCIDENCE OF THE NECESSITY FOR POSTOPERATIVE CATHETERIZATION

	GENERAL				SPINAL			
	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined
No. of cases	192	148	102	442	192	105	145	442
Catheterized once or twice	15.6%	14.8%	11.8%	*14.5%*	15.1%	12.5%	9.0%	*12.4%*
Catheterized more than twice	5.7%	4.0%	0	*3.8%*	4.1%	0	0	*1.8%*
Total cases requiring catheterization	21.3%	18.9%	11.8%	*18.3%*	19.2%	12.5%	9.0%	*14.2%*

Nurses' Bedside Notes.—In the herniorrhaphy series the nurses' comments on the bedside notes were reviewed and the results are seen in Table VI. It is believed that this is a valid approach to the patient's comfort during the postoperative period. It should perhaps be noted that no change in the nurses' routine has been instituted in this hospital since the earliest of the cases that comprise this report. The number of comfortable postoperative periods recorded is considerably greater following spinal anesthesia than following general anesthesia.

TABLE VI

NURSES' COMMENTS ON BEDSIDE NOTES IN THE HERNIORRHAPHY SERIES

	GENERAL	SPINAL
No. of cases	105	105
"Good day" or "Good night" (first 24 hours postoperative)	38.1%	58.1%
"Fairly good day" or "Fairly good night" (first 24 hours postoperative)	31.4%	24.8%

Urinary Protein and Casts.—Table VII shows a résumé of the study of the postoperative urinary findings, which includes only the herniorrhaphy series. The data are obtained from the rough estimations of protein and casts common to routine clinical urine examination, in which no quantitative studies

are made. There is a striking difference in the apparent effect of operation on the urine after the two types of anesthesia. Protein in the urine is increased after operation in nearly twice as many cases under general anesthesia as under spinal anesthesia. The number of casts in the urine is increased after operation under general anesthesia about five times as often.

TABLE VII

PERCENTAGE INCIDENCE OF CASES SHOWING INCREASES IN THE AMOUNT OF PROTEIN AND THE NUMBER OF CASTS IN THE URINE FOLLOWING OPERATIONS FOR HERNIA

	GENERAL	SPINAL
No. of cases	200	200
Increase in protein after operation	15.5%	9.0%
Increase in number of casts after operation	2.5%	0.5%

First Day of "Soft Diet."—Chart 1 shows the postoperative day on which "soft diet" was first ordered, as recorded in 400 cases of herniorrhaphy. There is a definite tendency for the cases that have had spinal anesthesia to be ready about 24 hours earlier for a diet approaching normal than the cases that have had general anesthesia.

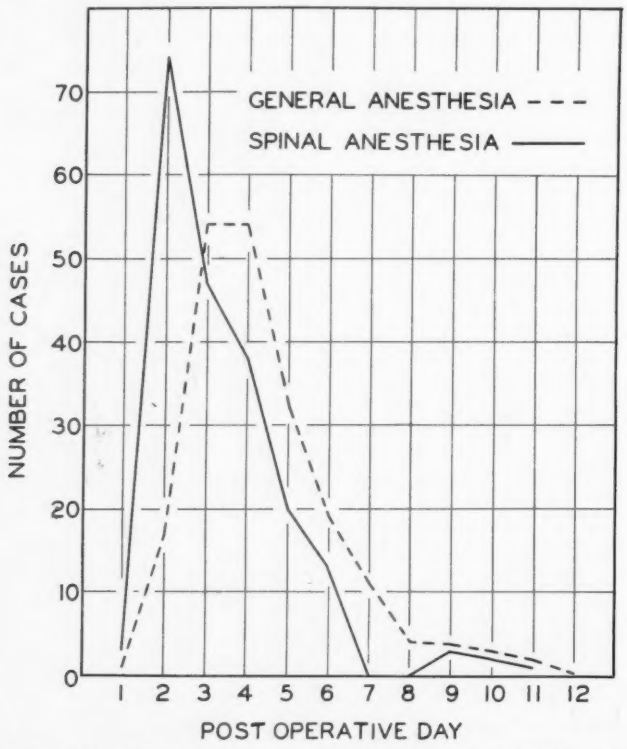


CHART 1.—Herniorrhaphy series: 200 cases under general anesthesia, 200 cases under spinal anesthesia. The curves show the number of cases on each postoperative day that were permitted to take "soft diet" for the first time.

Postoperative Complications.—In the group of 900 cases, the postoperative course of which has been recorded, postoperative complications were also studied (Table VIII).

In this limited group there was no instance of meningeal, cord, or root damage. Although the authors are not familiar with the entire group of 3,539 cases, only two instances of possible temporary damage to these structures are known. In one case there was a transient root pain which lasted only a few days, resulting from difficulty in entering the spinal canal in a case complicated by osteo-arthritis of the spine. The second case was one of temporary subjective muscular weakness of the legs without objective neurologic change, sensory or motor, and without sphincteric disturbances, a case having many of the earmarks of a functional condition.

It will be noted in studying Table VIII that the total recorded complications are slightly less frequent after spinal than after general anesthesia. The incidence of pulmonary complications is slightly greater after spinal than after general anesthesia, but most of this difference is accounted for by the high incidence of bronchitis following hysterectomy under spinal anesthesia, a curious phenomenon difficult to relate to the anesthetic. There is also a slightly greater incidence (seven cases as compared to six) of thrombophlebitis after spinal anesthesia than after general anesthesia. One case of coronary thrombosis occurred after spinal anesthesia for hernia. These differences are so slight as to be without significance.

TABLE VIII

INCIDENCE OF POSTOPERATIVE COMPLICATIONS

	GENERAL				SPINAL			
	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined	Herni-orrhaphy	Perine-orrhaphy	Hyster-ectomy	Com-bined
No. of cases	200	148	102	450	200	105	145	450
Bronchitis	3	6	2	11	2	2	10	14
Pleurisy	1	0	0	1	1	0	0	1
Pneumonia	1	1	2	4	1	2	2	5
Atelectasis	1	0	0	1	1	0	1	2
Pulmonary embolus	0	0	1	1	1	0	1	2
Total of pulmonary complications				18 *4.0%*				24 *5.3%*
Thrombophlebitis	1	2	3	6 *1.3%*	1	3	3	7 *1.5%*
Acute dilatation of stomach	0	0	1	1	0	0	0	0
Coronary thrombosis	0	0	0	0	1	0	0	1
Miscellaneous*	33	19	15		28	7	15	
Totals	40	28	24	92 *20.4%*	36	14	32	82 *18.4%*

* Includes those scattered diagnoses that do not seem to be related to anesthesia, such as disturbances of wound healing, psychoses, cystitis, drug rash, hiccough, measles, *etc.* A number of instances of transient cough and upper respiratory infection, not eventuating in bronchitis or pneumonia, are also included. See text for discussion of neurologic disturbances.

COMMENT.—Most of the figures presented herein show a slight advantage in favor of spinal anesthesia in relation to the behavior and comfort of the patients after operation. Data collected from the nurses' notes, and from the determination of the day on which a "soft diet" was ordered, present striking differences. These are great enough to offer evidence that the patient's course under spinal anesthesia is smoother than after general anesthesia, a conclusion that fortifies the established clinical impression. The less deleterious effect upon the kidneys after spinal anesthesia as compared to that after general anesthesia, as evidenced by the differences in postoperative urine examinations, deserves special emphasis. The surgeon is all too familiar with postoperative anuria.

The study of postoperative complications indicates that spinal anesthesia is not more dangerous from this point of view than is general anesthesia.

CONCLUSIONS

(1) The anesthetic mortality rate under spinal anesthesia in 3,539 cases is 0.028 per cent.

(2) A detailed study of 900 selected cases demonstrates that the postoperative course following spinal anesthesia is less disturbed than that following general anesthesia.

(3) There is no significant difference in the incidence of postoperative complications in 450 cases following spinal anesthesia as compared to 450 similar cases following general anesthesia.

(4) No serious disadvantages of spinal anesthesia have been demonstrated to outweigh its obvious and great advantages.

(5) Spinal anesthesia is a safe and satisfactory anesthetic under the conditions outlined, which include a proper selection of cases and a carefully controlled technic.

DISCUSSION OF THE PAPERS OF DOCTORS GUTHRIE AND LEHMAN

DR. R. H. JACKSON (Madison, Wis.).—I was very much interested in Doctor Lehman's paper and wish to congratulate him on his excellent presentation. We are, and have been for many years, using spinal anesthesia routinely, practically without exception in all of our abdominal surgery. Having administered it some 10,000 times, we find that there has been an appreciable reduction in mortality and a marked reduction in our postoperative complications during this period, attributable in great part, we believe, to the use of this agent.

We firmly believe that the sheet anchor of safety in the use of spinal anesthesia is unquestionably the administration of ephedrine in the proper amount, in the proper place, at the proper time, which is five minutes before the spinal tap by a needle long enough (not an ordinary hypodermic needle) to deposit it in the paraspinal muscle group which will insure its immediate absorption and protective action.

Whereas, formerly we did have numerous complaints from patients about postoperative headaches, *etc.*, of recent years these have been practically nil. A few days ago I asked our spinal anesthetist, Doctor Holmgren, to write down just why, in his opinion, we were having such routinely smooth admin-

istrations and how to avoid or relieve headaches. His recommendations were that one should:

(1) Use only small spinal puncture needles—No. 22 gauge. Postspinal tap leakage of fluid is less likely and possible trauma lessened.

(2) Take care to avoid loss of spinal fluid during the procedure.

(3) Keep patient flat in bed without a pillow for 24 hours. This is most important and should be explicitly followed without any exception to avoid headache.

(4) If, however, headache should develop, four minim doses of ephedrine, given intramuscularly and repeated two to four times at hourly intervals, generally give relief. If not, 1,000 cc. of one-half per cent normal saline solution, administered intravenously, almost always gives relief.

We have not had any postspinal paralysis or, of recent years, paresthesias. These, in our opinion, are due, when they occur, to: (1) Improper puncture technic or (2) some condition the patient had prior to the puncture.

We, therefore, never use spinal anesthesia on patients afflicted with any central nervous system disease, especially those due to syphilis. Nor do we use it in the hysterical type of individual or in those who present the slightest objection to its use.

Difficulty in Voiding.—This is probably more troublesome than with general anesthesia. We find that it is less so when we use pontocaine (which we are using with great satisfaction in prolonged operative procedures, such as gastric resection, biliary tract operation, *etc.*) in place of novocaine. In stubborn cases, instilling warm boroglycerine often initiates urination.

Backache, etc.—With the complete relaxation of spinal anesthesia and the patient lying on the back, the normal spinal curves tend to flatten out, giving rise to postoperative discomfort. This may be largely avoided by the placement of a small, hard pillow in the lumbar region. The table should always have a full length, two inch thick, soft rubber covering.

Use of Pontocaine.—For the past year we have, as I stated, used with great satisfaction this agent instead of novocaine, in all our anticipated protracted major abdominal procedures.

In general the same technic is used, including the pretap use of ephedrine. The few differences are as follows:

(1) Dosage of pontocaine: 2 cc. of a 1 per cent solution of pontocaine (that is, 20 mg.) are mixed with an equal amount of spinal fluid.

For cholecystectomy or in gastric surgery, the full dosage is given; that is, 4 cc. of mixed spinal fluid and drug. For lower abdominal work, 2 to 3 cc., in our experience, are sufficient.

(2) Site of puncture: For upper abdominal surgery, the puncture is between the first and second lumbar vertebrae, whereas, with novocaine, we have made it between the third and fourth.

(3) Rate of injection: Should be decidedly slower than with novocaine, one and one-half minutes being used to inject the 4 cc., a rate of about 25 seconds per cubic centimeter, whereas, with novocaine, it is five seconds per cubic centimeter.

(4) Smaller doses of ephedrine are sufficient. Thus 80 mg. is the maximum for a cholecystectomy, whereas, with novocaine it has been 100 mg.

Dr. John T. Moore (Houston, Tex.)—I firmly believe in spinal anesthesia both for the surgeon and for the patient who has to bear the brunt of the suffering. We use a good deal of spinal anesthesia in our work.

Backache is something I wish to say a word or two about. We find in traveling about and observing operations, that every few men have learned

to practice what Dr. Howard Kelly called attention to many years ago; namely, that we need to protect the back by supplying support. It is our practice to have three pillows: one under the head, one under the curvature of the back, and one under the flexure of the knees. As all of us know, who used to live on the farm and lay down on the floor to take a nap, that we were awakened in a few minutes with pain in the back and legs. Doctor Kelly arranged a rubber covered pad on the table to take care of that. We use three pillows in all operations, but in the lithotomy position we have to put the feet up, then we place a pillow under the back and one under the head. We have difficulty in getting these pillows into the operating room because none of the surgeons ever require them. Then again we have trouble in getting these pillows carried down with the patient on the stretcher. The pillow must go down with the patient, else you undo the good work accomplished on the table. When the support to the back and legs is not provided and you ask the patient how he feels he will say, "Fine, but I have a terrible backache and leg ache." There is no need in having patients suffer in that way. I think 7 per cent had backache in Doctor Lehman's splendid series and this could have been reduced to less than 1 per cent.

Dr. Frank H. Lahey (Boston, Mass.).—Because spinal anesthesia has been such a controversial subject, and because we have been advocates for it, I think I should say something of our views and experiences with spinal anesthesia. I am sure Doctor Jackson will not be offended when I say that ephedrine is an excellent drug, but I would put the sheet anchor of safety beyond that and say it is in the anesthetist. We have certain convictions about spinal anesthesia. One is that I believe it is an extremely dangerous plan for the surgeon to give the spinal anesthetic and then turn the anesthesia over to a nurse or to an inexperienced man. We have given several thousand spinal anesthesias and I do not care how well trained the man may be, one will occasionally creep too high. We have had three respiratory paralyses. This is well handled in the hands of men who are competent to spot this paralysis early and use oxygen until the anesthesia wears off. In the hands of nurses and inexperienced anesthetists some of these patients will die needlessly. Furthermore, it is important that these men be experienced not only in the anesthetic but in the dose of the anesthetic, and also whether it be a heavy or a light solution. That, I believe, plays a very important part. We have three drugs that we use: Novocaine, now used very little; protocain for anesthesias up to two hours, and nupercaine for anesthesias up to five hours. This latter drug was formerly considered very dangerous, and may well be so, unless one understands it thoroughly. Doctor Jones of London, England, developed a dilute solution of nupercaine which is not yet available to the public but we have now used it for two years and I think it will be the ideal anesthetic. In a solution of 1:1,000 or 1:1,500 it will provide three to five hours of anesthesia. Just before I came down here I operated upon a case that took five hours, and the relaxation was just as good at the end of the operation as at the beginning. By placing the patient on the face, inclined upward, and with the neck sharply flexed, nupercaine will provide complete motor root relaxation and the patient can be carried through these long procedures with complete success.

One final thing, and I feel very strongly about this, and that is that medical schools are extremely lax today in teaching anesthesia. That fact will be forced on us whether we like it or not.

Some of the developments in anesthesia are so striking that they may well be mentioned. For instance, Dr. A. E. Guedel of Los Angeles has de-

veloped a method whereby carbon dioxide may be so washed out of the lungs that breathing entirely ceases, respiration being entirely carried on by the to-and-fro method of squeezing and expanding the bag filled with oxygen and the anesthetic mixture. This provides complete relaxation of the diaphragm, quietness of the mediastinal partition, and quietness of the lungs, and is of great value particularly in operations for diaphragmatic hernia and those within the chest. We have had our anesthetists carry patients for one-half to three-quarters of an hour without breathing voluntarily themselves at any time, and whenever we were ready, they have thrown into the breathing circuit a dose of carbon dioxide which promptly stimulates voluntary respiration and breathing goes on regularly.

Another interesting development is that the anesthetists now provide, for the chest surgeons, intratracheal catheters with a curve on the end of them and a balloon surrounding the end so that the curved end of the catheter, introduced through the trachea under the laryngoscope, enters the main bronchus of the lung opposite the one to be removed. The balloon is then blown up so that all of the anesthetic is carried on into the good lung. Think how valuable this is in those patients with tuberculosis or bronchiectasis, so that contamination of the good lung can be prevented; and likewise, we have been able to demonstrate conclusively, in operations performed by Doctor Overholt, of total pneumonectomy, that when the main bronchus of the lung to be removed is cut off, no air escapes, proving that the catheter with the balloon on it inserted in the opposite main bronchus is tight.

When we realize how many tracheotomies are performed, and how many of these could be avoided if we had trained anesthetists, then I think we are aware of how necessary it is to improve our anesthesia and to train more anesthetists.

It takes time and material to train anesthetists, and we with a large material are only able to train two a year, but we are training them and placing them over the country where we hope they will help to elevate the standard of anesthesia. There is a good deal of slack to be taken up, as I have repeatedly said, in anesthesia, and medical schools must, I think, pay more attention to playing their part in taking this up.

Dr. Harold L. Foss (Danville, Pa.).—A year or two ago, at a meeting of the American Medical Association, one of our most distinguished American surgeons read a paper on spinal anesthesia, the gist of his remarks being that anyone using it was engaged in malpractice. I asked him afterward if he had ever used it and he said, "Never, thank God!" Here was one of our best known educators talking dogmatically about a subject concerning which he knew nothing.

I thoroughly agree with what Doctor Lehman has said and think his analysis of postoperative spinal results is the most complete that has been made so far. Two or three years ago, desiring to know just where we stood with our own work, I made a comparative study of a series of our general and spinal anesthesia cases. To make a study that would be fully comparable, I took a series of patients all operated upon by myself, with the same operating team and same pre-and postoperative treatment. The study was made of patients operated upon under general anesthesia, mostly ether and gas, and other under spinal anesthesia, limiting them to major cases and to operations below the diaphragm. There were 2,000 operations under spinal, with a mortality of 6.5 per cent, and 2,000 under ether or ether-ethylene anesthesia with a mortality of 6.8 per cent. The average dose in the spinal cases was 133 mg. of novocaine, never exceeding 200 mg.

We were interested in *when* death took place. It has frequently been reported that, when spinal anesthesia is used, a formidable number of deaths occur within the first ten or 12 hours. We found this not to be true. At the end of the third day there had been 46 deaths under spinal, and 58 under gas-ether anesthesia. There were more deaths at the end of 12 hours under general anesthesia than under spinal; even after five days the same held true. We have now used spinal anesthesia in about 3,900 cases, with but one operating room death, and that patient had an extensive miliary tuberculosis with coronary occlusion. During the same period, with the same number of general anesthesia cases, there were four operating room deaths.

We asked the patient how he felt about it. A questionnaire was sent to 500 who were asked, if they had to be operated upon again, would they choose spinal or gas-ether anesthesia. But 11 per cent voted for the latter. Of a large group having had both general and spinal in earlier operations, 70 per cent stated that they would choose spinal if they had to be operated upon a third time.

Spinal anesthesia is a subject into which too much prejudice and partisanship has crept, displacing impartial, accurate and scientific analysis of the danger of the procedure on the one hand and its manifold advantages on the other. It is not a method to use routinely; per contra, neither is inhalation anesthesia, local, rectal, or intravenous. In the course of a year the surgeon who gives his patient every possible advantage and consideration will use several methods of rendering them insensible to pain, and among those used, and frequently so, should be spinal anesthesia.

While the latter procedure is safe, its administration must be in the hands of a skilled person who is meticulous in his technic, pursues absolute asepsis, uses the smallest needle (No. 22 gauge or smaller) and keeps them constantly sharp by the use of a jeweler's oil stone, limits his dosage to 200 mg. or less, and uses only the best medium which, in our experience, has been neocaine.

Dr. Hubert A. Royster (Raleigh, N. C.).—I wish to mention just three points: First, you can prove anything by statistics. Second, I do not think any surgeon has a right to attribute any death on or after the fifth day to any type of anesthesia. Third, as a group of surgeons, which would you prefer if you had to be operated upon? Let's have a show of hands: Would you prefer spinal or a general anesthesia? (The showing of hands resulted in 10 to 1 in favor of general anesthesia.)

Dr. Rudolph Matas (New Orleans, La.).—The subect of Doctor Lehman's paper, "Spinal Anesthesia," recalls the fact that it was about 37 years ago that the first recorded operation under spinal anesthesia in the United States was performed in my service at the Charity Hospital, New Orleans. This coincidence would seem to justify a momentary glance at the history of this event. It was in April, 1899, that Bier, of Kiel, rediscovered and recast the forgotten technic of spinal anesthesia, which Leonard Corning, of New York, had first described in 1885. Much impressed by Bier's results and the still more surprising achievements of Tuffier, of Paris, I administered my first spinal injection on November 19, 1899, using eucaine b for this purpose, but the resulting anesthesia was unsatisfactory. One month later, on December 18, 1899, I renewed the attempt with cocaine, using 1 cc. of a 1 per cent solution, repeated in five minutes, injecting it between the third and fourth lumbar vertebrae. The result was extraordinary. Not only a complete anesthesia below the waist followed, but the loss of sensibility gradually extended to the neck and head sufficiently to allow these parts to

be pricked and pinched without pain. The operation—a hemorrhoidectomy—was performed with the patient in the lithotomy position with pelvis high up. This position probably accounts for the widely diffused anesthesia, which, at the time, gave me considerable anxiety in fear that it would extend to the medulla, with fatal consequences. Fortunately, nothing happened and the patient recovered, but not without the headache, backache, vomiting and febrile reaction which further experience was to teach us was the most frequent consequence of the cocaine injections. This operation was recorded in the Journal of the American Medical Association (December 30, 1899), and preceded by several days the first trial of the method, in Chicago, by Dr. J. B. Murphy, who gave it a powerful impetus in the West.

The results of the first trials of spinal cocainization were so remarkable from the analgesic point of view, that I was about to publish my first 50 cases, when a series of accidents occurred in the last three—one an abdominal hysterectomy for fibroid, in which the patient was saved only by persistent efforts at artificial respiration; another, followed by a chill, acute backache with hyperpyrexia of 105° F., and a third, by a violent headache and backache which persisted for several weeks. These cases, following in rapid succession, considerably moderated my enthusiasm and led me to realize that the dangers of spinal anesthesia with cocaine could not possibly be compensated by the simplicity of the technic or the effectiveness of the anesthesia. This led me, in company with a number of other pioneers in the United States, to abandon spinal anesthesia with cocaine altogether, substituting tropacocaine, stovaine, but always with great hesitation, until novocaine (percaine, neocaine) was introduced by Braun, in 1905–1906, when the lower toxicity of this anesthetic and relative freedom from marked meningeal reactions brought me back to spinal anesthesia, but always with discrimination according to indications, and only for operations below the diaphragm.

We can readily understand that a method which is capable of providing such complete and relaxing anesthesia of the abdomen and its contents, and accomplishes this great desideratum with simplicity of technic and a minimum of apparatus and assistance; which dispenses with the services of a trained anesthetist, often permitting an intern to make the injection while the surgeon washes his hands, should be captivating to many surgeons who, in successfully attaining the main objective of the operation, regard as negligible the postanesthetic headaches, nausea, vomiting and obstinate backache that so often complicate and delay the recovery of the patient.

It is remarkable that, after 37 years of experience in spinal anesthesia, the profession is still engaged all over the world in lively discussions and debates on its relative merit in comparison with other methods of anesthesia. It is also remarkable that the great favor with which spinal anesthesia has been received in many quarters has been equally denied in many others.

The facts are that, despite the innumerable methods and suggestions that have been devised to control the action of the anesthetic, to limit the field of the anesthesia, and despite the advantages claimed for percaine or neocaine, tutocain, spinocaine, neothesin and other numerous claimants to special favor in this field, we know that the ideal of safety has not been attained. The stress laid on possible emergencies caused by circulatory and respiratory failure, by bulbar paresis and arterial hypotension, and the prevention of these accidents by the coincident administration of ephedrine, strychnine, caffeine and intravenous saline infusions, is proof enough that spinal anesthesia, despite the enormous progress that has been made in its indications, in its technic and mode of action, still contains potential and unpredictable factors of danger that are far from negligible in its practice. On the other

hand, it is a question whether a *conscient* surgical analgesia, obtained by spinal "splanchnic," and epidural or "segmentary" injections, will be able to cope with the constantly improving anesthetic gases and safety devices that are now making general narcosis safe and more efficient for the major operations of surgery, with practical freedom from the dangers and complicating sequelae that made ether and chloroform so objectionable in the past.

While the words "dangerous" and "safe" are purely relative terms when applied to qualify anesthetics which produce anesthesia by temporarily inhibiting the functions of either the brain or spinal cord, or both, in their external relations, we must realize that in so far as general narcosis is concerned, the times have changed and it is increasingly difficult to deny the great boon of modern synergistic anesthesia with gas (e.g., ethylene-oxygen sequences) and preliminary sedation, on the score of the greater danger of these gases, when the accidents and sequelae of spinal or "splanchnic" analgesias are taken into consideration.

Therefore, and despite my long and consistent record as a pioneer and advocate of local, regional and spinal anesthesia, I now feel that I must join the Fellows who, in response to Doctor Royster's motion, and in a large majority, signified their choice of the sleep of general anesthesia in preference to the conscious wakefulness of spinal analgesia when applied to themselves and in equality of circumstances.

BRIEF COMMUNICATIONS AND CASE REPORTS

HERNIA OF THE VERMIFORM APPENDIX *

WILLIAM JOHN RYAN, M.D.

PHILADELPHIA, PA.

FROM THE DEPARTMENT OF SURGERY, ST. MARY'S HOSPITAL, PHILADELPHIA, PA.

THREE consecutive cases of hernia in which the appendix was found in the sac at operation prompted a review of the literature and of the cases of hernia operated upon at St. Mary's Hospital.

ABBREVIATED CASE REPORTS

Case 1.—J. H., male, age 53, gave a history that after lifting a heavy door six weeks before admission, he noted a swelling in the right inguinal region which had increased in size. On admission, there was found a right, indirect, complete inguinal hernia with more tenderness than one would expect on examining such a condition. At operation, the hernial sac contained an acutely inflamed appendix which was removed and a Bassini herniorrhaphy was performed. Recovered.

Case 2.—Mrs. R. E., age 53, was admitted with an incarcerated, right femoral hernia. Operation was performed immediately under spinal anesthesia. The abdomen was opened through a low McBurney incision. The femoral opening was enlarged from within to facilitate reduction of contents of sac. These proved to be a segment of cecum and proximal half of the appendix. The cecum was not completely obstructed (Richter's hernia). The cecum and appendix were of a dark purple color. Upon application of heat, however, their color returned to normal. The appendix was removed and the abdomen closed after placing a purse string suture around the femoral opening. Recovered.

Case 3.—A male, age 50, was admitted complaining of a swelling in the right inguinal region which had been present for six months, but which had become painful during the last few days. Diagnosis: Right, incomplete, indirect inguinal hernia. At operation an incomplete, indirect, right inguinal hernia was found with the appendix in the sac. The appendix was swollen and the superficial vessels were injected. The cecum helped form the anterior or outer wall of the sac. The appendix was removed and a Halsted herniorrhaphy was performed. Recovered.

Hernia of the appendix is a protrusion of the appendix through a normal or abnormal opening in the abdominal wall or in the pelvis. It is not common and usually occurs past middle age. It is usually accompanied by the cecum, omentum or small bowel. An isolated hernia of the appendix is more usually found in young children.

The first report of an operation for hernia of the appendix that we have been able to find was by DeGarengrot,[1] in 1731, and this case was operated upon, not for hernia nor for appendicitis, but for what was thought to be an abscess in the inguinal region. The next report was by Amyard in 1736, which was followed by a report of Morgagni in 1761. In 1785, Hevin[2] de-

* Read before the Philadelphia Academy of Surgery, December 2, 1935. Submitted for publication September 16, 1936.

scribed in detail an operation for suppurative appendicitis in a femoral hernia. Frolichter, in 1806; Hesselbach, in 1814; Saramelli in 1835 and Javanelli in the same year, all reported individual cases. In 1836, Merling described an operation which was performed for strangulated hernia of the appendix. Charyard, in 1837, and Cabaret,[3] in 1842, also operated for hernia of the appendix. During this early period, operation was performed only for treatment of the abscess which had formed and the procedure was simple incision and drainage. In the latter half of the nineteeth century, and with the advent of antiseptic surgery, operation was performed earlier but unless the appendix was gangrenous or the seat of an acute suppurative inflammation, it was reduced into the abdomen and the hernia repaired.

A. C. Wood,[9] in 1906, reviewed the literature of 3,054 cases of herniae in which the appendix alone or with other viscera was found 58 times, or 0.19 per cent.

Gray,[13] in 1910, collected 58 cases and reported one of his own. He concluded that strangulation is more apt to occur in femoral hernia—75 per cent—and appendicitis in inguinal hernia—55 per cent. The diagnosis rests on symptoms and local signs. Death occurred in seven cases due either to failure to recognize the insidious nature of the condition or to attempts at reduction by taxis.

Coley,[14] in 1910, reported 2,200 hernia operations in which the appendix alone was found in ten; the cecum and appendix in seven.

The most comprehensive study of the subject was by Leigh Watson,[15] in 1923. He collected from the literature 512 cases of hernia of the appendix, with the following statistics:

Inguinal	269
Femoral	217
Obturator	2
Site not given	24
In 242 Inguinal: Male	218
Female	24
Side involved in 249: Right	230
Left	19

Of the cases of inguinal hernia operated upon the:

Appendix was excised in	140 with 5 deaths
Appendix reduced in	17 with 2 deaths
Herniorrhaphy plus appendicectomy by additional incision in	38 with 1 death
Abscess drained in	26 with 6 deaths

Of the femoral herniae operated upon:

The appendix was alone in 175	
Of the operated cases	177 were females
	4 were males
Appendix was excised in	129 with 5 deaths
Appendix was reduced in	23 with 2 deaths
Abscess drained in	22 with 9 deaths

He further stated that the herniated appendix was found in:

Inguinal hernia	55%
Femoral hernia	40%
Umbilical hernia	4%
Obturator hernia	0.4%

In ventral and diaphragmatic hernia it is most always accompanied by other viscera.

Watson, in his review of the literature, shows that the appendix is present in 1 to 1.5 per cent of all herniae containing abdominal viscera; 1 per cent between the ages of 30 and 50 years and 1.5 per cent past the age of 50. Isolated hernia of the appendix was comparatively rare, occurring three times in 1,000 herniae. Since Watson's study there have been published 12 reports of isolated cases:

9 Right inguinal	—appendix alone in 6
	appendix and cecum in 3
2 Left inguinal	—appendix and cecum in both
1 Femoral	—appendix alone

As to the comparative frequency of abdominal and hernial appendicitis, Sonnenburg, Hoffman and Fromme collected separate statistics and these, when totaled, showed that in 8,692 cases of appendicitis the appendix was found in a hernial sac in 11 or 0.13 per cent. In the 512 cases of hernia of the appendix collected by Watson, symptoms of appendicitis were present in 124, but the pathologic findings were not given.

To these statistics we add the following from the records at St. Mary's Hospital, Philadelphia, from July 1, 1939, to June 30, 1934. Five surgeons operated upon 193 cases of hernia. Of these:

148 were indirect inguinal
28 were direct inguinal
11 were femoral
3 were umbilical
3 were incisional
All were adults past 30 years of age

Not including the three cases already noted the:

Appendix was found alone in three inguinal and in one femoral hernia.

Appendix and omentum	1
Appendix, cecum and bladder	1
Appendix and cecum	1

In the cases in which hernia of the appendix alone was found, the pathologic report of the appendix was as follows:

Femoral—1 case —acute suppurative appendicitis
Inguinal—3 cases—acute suppurative appendicitis in two and no report in one.

Probable Method of Occurrence.—Coley believes that in practically all cases of indirect inguinal hernia there is an open funicular process or

pouch of peritoneum present at birth, and quoting Carnett,[12] reveals three ways that congenital hernia of the cecum or appendix may originate:

(1) The mobility of the cecum and its proximity to the internal ring easily permits its entrance into a patulous vaginal process either before or after birth, forming a congenital inguinal hernia.

(2) It may be drawn actively into the vaginal process by means of its excessively developed connections with the testicle.

(3) When the cecum descends to the iliac fossa as early as the fourth fetal month, adhesions may form between the cecum and appendix and the posterior parietal peritoneum covering the testes or gubernaculum. The subsequent descent of the vaginal process and testis will draw the cecum or the cecum and the appendix into the inguinal canal forming a congenital hernia. Carnett in referring to cecal herniae classified them as: (1) simple and (2) gliding. We are in accord with this classification as evidenced by Case 3, in which the cecum formed the anterior or outer wall of the hernial sac.

SUMMARY.—A fairly intensive review of the literature reveals 524 cases of hernia of the vermiform appendix, either alone or accompanied by one or more abdominal viscera. To this number we are adding ten cases which occurred in 193 consecutive herniorrhaphies. Of these ten, the appendix was alone in six—five inguinal and one femoral; the appendix and omentum in one case; the appendix, cecum and bladder in one case; the appendix and cecum in two cases. After completion of the present article, on reading Shawan and Altman's[22] article in the ANNALS OF SURGERY for May, 1935, we note that in 97 femoral herniae the appendix was found in the sac three times. This brings the total number of cases that we have been able to find up to 537.

REFERENCES

[1] DeGarengrot: Traite des operations de Chir., **1**, 237, 1731.
[2] Hevin: Cours de Path. et de Therap. Chirurgicale, 407, 1785.
[3] Cabaret: Jour. connaissances medico-chirurgicales, **10**, 54, 1842.
[4] Coley, quoted by Hill, L. L.: Med. Rec., **56**, 303, 1899.
[5] Peterson, R.: J.A.M.A., **33**, 1407, 1899.
[6] Jopson, J. H.: University Medical Magazine, 1900.
[7] Sheldon, J. G.: Amer. Med., **6**, 668, 1903.
[8] DeGarms, W. B.: Tr. Med. Soc. Virginia, 152, 1904.
[9] Wood, A. C.: ANNALS OF SURGERY, **43**, 688–703, 1906.
[10] James, G. S.: Iowa Md. Jour., **15**, 472, 1908.
[11] McEwen, J. A. C.: ANNALS OF SURGERY, **49**, 516, 1909.
[12] Garnett, J. B.: ANNALS OF SURGERY, **49**, 491, 1909.
[13] Gray, H. T.: Brit. Med. Jour. **2**, 1142, 1910.
[14] Coley, W. B.: Progressive Med., **2**, June, 1910.
[15] Watson, Leigh: Hernia, C. V. Mosby, 527, 1924.
[16] Burne, T. W. H.: Brit. Med. Jour., 96, January, 1926.
[17] Pirie, A. J.: Brit. Med. Jour., 373, February, 1926.
[18] Foster, S.: Brit. Med. Jour., March, 1926.
[19] MacMillan, J. A. and F. B.: Jour. Michigan State Med. Soc., **26**, No. 3, March, 1927.

MacMillan, J. A. and F. B.: Military Surg., **63**, No. 1, 77, July, 1928.
[20] Brooks, J. D.: United States Veterans Med. Bull., **5**, 801, October, 1929.
[21] Edelen, C. M.: Kentucky Med. Jour., **28**, 349, 350, July, 1930.
[22] Shawan, H. K., and Altman, Raphael: ANNALS OF SURGERY, **101**, 5, 1270, May, 1935.

MALIGNANT DIFFUSE GASTRIC POLYPOSIS

FREDERICK CHRISTOPHER, M.D.

EVANSTON, ILL.

FROM THE SURGICAL SERVICE OF THE NORTHWESTERN UNIVERSITY MEDICAL SCHOOL AND EVANSTON HOSPITAL, EVANSTON, ILL.

MENETRIER'S[1] classification of the condition of gastric polyposis into two groups has been generally accepted. The first group, "polyadenomes polypeux," is the most numerous one and includes those cases in which there are discrete polyps with independent attachments—in one instance 300 were found. The second group, "polyadenomes en nappe," comprises the cases in which the polyps arise from a thickened plaque like base, and are so closely packed in rows as to resemble somewhat the convolutions of the brain (Briquet). Kirklin and Broders[2] state that "To Menetrier's exhaustive description, little can be added. In view, however, of the marked difference in the gross appearance of the two varieties as well as the histologic differences in the glands, and the great rarity of the second variety, we incline to the opinion that he might better have given the latter an independent pathologic status." Broders has suggested this condition be termed "polypoidosis." Strauss, Meyer and Bloom[3] state that there were only five such cases reported up to 1928 and they add two cases. According to Kirklin and Broders[2] there are probably about five other cases. The case reported by Balfour[4] is a particularly good example.

In their careful study of diffuse gastric polyposis in 1926, Brunn and Pearl[5] collected 84 cases of both varieties of diffuse gastric polyposis of this condition and added five cases of their own. These authors found malignant degeneration to be present in about 12 per cent of the 84 collected cases.

The following case is of interest because it not only belongs to Menetrier's rare second group but it had also undergone malignant transformation.

Case Report.—H. P. R., age 55, was admitted to the service of Dr. Geo. C. Turnbull at the Evanston Hospital June 14, 1936. In spite of an excellent appetite he had lost 12 pounds in the last year and during this time fulness and distress in the lower abdomen had become progressively worse. Constipation had been present for the previous six months. The history otherwise was negative. The patient was fairly well nourished and the physical examination negative. On admission, the erythrocytes were 4,040,000. Hemoglobin, 76 per cent. Leukocytes, 7,800. Urine, negative. The blood Wassermann and Kahn were negative. The stomach contents contained no free acid. Roentgenologic examination showed what was thought to be a rather large carcinoma of the stomach (Fig. 1).

Submitted for publication December 26, 1936.

Exploratory laparotomy June 23, 1936, demonstrated no definite hard tumor, but the wall of almost the entire stomach was found to be markedly thickened but quite soft and

FIG. 1.—Roentgenogram of stomach before operation, suggesting a rather large carcinoma involving the body of the stomach.

FIG. 2.—Photograph of the resected portion of the stomach with the mucosal surface everted, showing the enormously thickened rugae. The pyloric end is at the right of the figure.

pliable. The stomach was opened and the mucosa was found to be irregularly hypertrophied, soft, and friable, and had the appearance of irregular, thick red plush (Fig. 2).

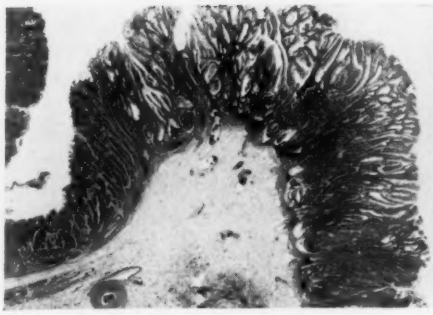


FIG. 3.—Photomicrograph of gastric musoca and submucosa. The glands are elongated and distorted in all portions and in the upper right portion of the figure shallow invasion of the fibrous layer is shown. Inflammatory changes are very slight (low power).

FIG. 4.—Photomicrograph of mucosa and submucosa in another area. Typical glandular elements have invaded the fibrous wall well beyond the muscularis mucosa. Some of these are distended to form irregular small cysts. No normal mucosa remains.

FIG. 5.—Roentgenogram after resection of the stomach. Note gastrojejunal stoma.

The liver was apparently normal. There were one or two palpable lymph nodes. A subtotal resection of the stomach by a modified Pólya method was carried out. Only two or three inches of the cardiac end of the stomach remained. 500 cc. of blood were given during the operation. After a stormy convalescence, including a wound disruption, the patient recovered and was discharged August 5, 1936.

Pathologic Examination.—Gross: Dr. F. D. Gunn. The specimen (Fig. 2) consisted of part of the wall of a stomach including all of the pyloric portion and a large part of the cardiac portion. After fixation in Kaiserling's solution it measured about 18 cm. in length along the greater curvature and 17 cm. in maximal circumference. A few tags of omental tissue were attached along the lesser and greater curvature but no lymph nodes could be found. The serosal surface contained a few small superficial hemorrhages but was not otherwise remarkable. With the exception of a narrow margin at the proximal end and of the lining of the pylorus, the entire mucosa was enormously thickened, the rugae measuring up to 2 cm. wide and 1.5 cm. deep. On surfaces made by incising the mucosa, the thickened membrane measures up to 8 Mm. in thickness. There was no apparent ulceration of any part of the mucosa and with the exception of the normally thin membrane at the two ends of the specimen, the hypertrophy appeared to be of about the same degree at the proximal and distal ends and at the greater and lesser curvatures.

Microscopic Diagnosis.—Diffuse adenocarcinomatous metaplasia of the gastric mucosa with shallow invasion of the submucosa in several places (Figs. 3 and 4). No point of origin could be determined. The degree of anaplasia was much the same throughout the stomach.

On December 1, 1936, the patient had gained ten pounds and was back to work. He was eating a well balanced diet in three medium sized meals a day plus extra feedings. A preexisting hypertension seemed to have been somewhat increased as a result of the operation. An incisional hernia was well controlled by an abdominal support.

REFERENCES

[1] Menetrier, P.: Arch. de physiol. norm. et path., **1, 32,** 236, 1888.

[2] Kirklin, B. R., and Broders, A. C.: J.A.M.A., **98,** 95, January 9, 1932.

[3] Strauss, A. A., Meyer, J., and Bloom, A.: Am. Jour. Med. Sci., **176,** 681, November, 1928.

[4] Balfour, D. C.: Surg., Gynec., and Obstet., **28,** 465, 1919.

[5] Brunn, H., and Pearl, F.: Surg., Gynec., and Obstet., **43,** 559, November, 1926.

[6] Versé, M.: Arbeiten aus dem Patholog. Inst. 2 u Leipzig, 1908. Verlag von S. Hirzel.

[7] Ewing, Jas.: Neoplastic Diseases. 3rd Ed., W. B. Saunders Co., 688, 1928.

[8] Myer, J. S.: J.A.M.A., **41,** 1960, November 29, 1913.

[9] Douglas, J.: Annals of Surgery, **77,** 580, 1923.

[10] Heinz, H.: Beitr. Z. klin. Chir., **93,** 228, 1914.

[11] Brams, W. A.: Med. Clin. N. Amer., **8,** 533, 1924.

[12] Ruggles, H. E.: Am. Jour. Roentgenol., **7,** 356, 1920.

[13] Bryan, L.: Southwestern Med., **6,** 223, 1922.

[14] Sielmann, R., and Schindler, R.: Fortschr. a. d. Geb. d. Roentgenstrahlen., 33, 191, 1925.

[15] McPhedran, A.: Canad. Med. Assn. Jour., **11,** 524, 1921.

[16] Galdan, D., and Pop, A.: Fortschr. a. d. Geb. d. Roentgenstrahlen, **35,** 270, 1926.

[17] Cameron, G. R., and Wright-Smith, R. J.: Med. Jour. Australia., **2,** 258, 1927.

[18] Rigler, L. G.: Am. Jour. Surg., **8,** 144, 1930.

THE VALUE OF ZINC PEROXIDE IN THE TREATMENT OF CHRONIC UNDERMINING BURROWING ULCER

DUE TO THE MICRO-AEROPHILIC HEMOLYTIC STREPTOCOCCUS

GRANT P. PENNOYER, M.D.

NEW YORK, N. Y.

THE value of zinc peroxide in the treatment of certain anaerobic infections has been advocated by Meleney.[1] The dramatic cure of the appended unusual case by the use of this chemical seems worthy of publication. Zinc peroxide is a white powder, insoluble in water, which has the ability when in contact with water or wound exudate to liberate oxygen over a long period of time, leaving behind zinc oxide. A wound thoroughly packed with this substance is saturated with nascent oxygen which seems sufficient in many cases to overcome anaerobic infections. Not all samples of the drug are capable of liberating oxygen and it is important to select an active preparation. This is easily demonstrated by suspending a little of the white powder in a test tube of water and allowing it to stand over night. A worthless preparation is unchanged, staying in the bottom of the tube as an insoluble heavy white powder, while an active one will be all puffed up by numerous bubbles of oxygen which keep rising slowly to the surface of the water.

Case Report.—R. H., B-362301, female, age 7, was referred March 28, 1936, to the Children's Surgical Ward of Roosevelt Hospital by Dr. Alexander T. Martin, suffering from a peculiar spreading ulceration of her right neck and cheek of eight months' duration. Fig. 1 shows its extent and location. The process had started eight months before as an inflamed indurated nodule in the skin of the neck just below the angle of her jaw. It was thought to be a simple pyogenic infection and after ten days of conservative treatment without improvement, it was incised. A small amount of thin, sanguineous pus was evacuated. Instead of healing like an ordinary abscess, the area of inflammation extended slowly and a small fluctuant area appeared about 3 cm. in front of the original lesion, which was also incised. Meanwhile, the original incision continued to drain and the edges began to ulcerate slowly. It was then noticed that the two incisions were connected by a sinus beneath the skin. The edges of the second incision ulcerated slowly until finally the openings became confluent, forming a single ulcer with deeply undermined edges. Despite local treatment with antiseptic ointments and solutions, the lesion gradually increased in size for eight months until it had reached alarming proportions on admission to the hospital. It was thought to be a case of tuberculosis of the skin and the child was given supportive general treatment. In the fifth month, she had four roentgen ray treatments at ten day intervals, each exposure being three and one-half minutes, the dosage being 5 milliamperes, with a nine inch spark gap, ten inches distant, with a 3 Mm. aluminum plate filter, with no apparent improvement. Ultraviolet light also had no effect on the lesion.

Examination showed a very large ulcer with a base of sluggish, almost gray granulation tissue and edges undermined as much as 2 cm. in places. The margins of the ulcer extended from the lower lobe of the ear upward on to the cheek for 3 cm., then downward and forward to the middle of the body of the right mandible, thence irregularly downward to the middle of the sternomastoid muscle, thence backward on to the posterior triangle of the neck to a point 3½ cm. behind the ear. There was no associated enlargement of the lymph nodes. The general health of the child seemed to be unaffected. She had no fever. She was normally developed and nourished for her age and physical

Submitted for publication January 7, 1937.

examination revealed no other pathology. Her past history was irrelevant and there was no evidence of any focus of infection in her throat. Her tonsils and adenoids had been removed one year previous to the onset of her present trouble. An older brother and both parents are living and well and there is no history of tuberculosis or exposure to it.

Careful laboratory studies were made. Two Mantoux tests for tuberculosis were negative. The Wassermann reaction was negative. Roentgenologic examination of the chest showed a slight increase of the hilum shadows of the lung but no evidence of

FIG. 1.—Showing extent of ulcer before treatment was started.

FIG. 2.—After ten days' treatment with zinc peroxide.

tuberculosis. There was no secondary anemia or increase of the leukocyte count, and blood smears were normal. The urine was negative. Exudate from the undermined edges of the ulcer and the necrotic base contained no tubercle bacilli, but produced a pure culture of hemolytic Streptococcus. Biopsy at the edge of the ulcer showed acute inflammatory tissue without any evidence of tuberculosis or malignancy. After being in the

FIG. 3.—Ulcer after three weeks' treatment.

FIG. 4.—Ulcer six months later. Scar has contracted.

hospital for two weeks, during which time the lesion was being treated with antiseptic ointments, the case was seen in consultation by Dr. Frank Meleney who demonstrated that the Streptococci cultured from the ulcer grew very much more luxuriantly under anaerobic conditions and suggested the use of zinc peroxide.

Treatment with zinc peroxide resulted in immediate and dramatic improvement. In view of the fact that the lesion had been gradually and continually extending for eight

months, there was no possible doubt that the zinc peroxide was the curative factor. A preparation of zinc peroxide, which in a few hours actively formed oxygen bubbles on being suspended in water, was selected. Sufficient hydrogen peroxide was added to make a thin paste. Narrow gauze packing was thoroughly impregnated with this mixture and the whole wound very carefully packed, taking especial care that it was very thoroughly applied into every recess underneath the undermined skin. Several layers of vaseline gauze were then placed over the whole region to seal the dressing and prevent evaporation. Dressings were changed daily. The only surgery which was performed was to open one or two burrowing areas underneath the skin and trim off the deeply undermined edges. The Streptococci disappeared from the base about ten days after treatment was instituted. As soon as the infection was under control, epithelium began to grow out from the edges of the ulcer and the granulating base took on a healthy red appearance. The patient was discharged, healed, four weeks after the institution of treatment with zinc peroxide. Figs. 2, 3 and 4 illustrate well the stages of healing.

SUMMARY.—This unusual case is reported to emphasize the value of zinc peroxide in the treatment of chronic undermining ulcers due to the microaerophilic hemolytic Streptococcus. Its success depends upon the constant liberation of oxygen over a long period of time, and it is most important to use a preparation of zinc peroxide which liberates oxygen actively after being suspended in water a few hours.

REFERENCE

[1] Meleney, Frank L.: Surg. Clin. N. Amer. 16, No. 3, 691-711, June, 1936; ANNALS OF SURGERY, **101**, 997–1011, 1935.

PRIORITY FOR THE "EXTERIORIZATION OPERATION" FOR CARCINOMA OF THE BOWEL

MAX THOREK, M.D.

CHICAGO, ILL.

IN DISCUSSING the exteriorization procedure for attacking carcinoma of the large bowel and alluding to this procedure as the "Mikulicz operation," Dr. Fred W. Rankin called my attention to the fact that the credit for priority in this operation belongs to Dr. Oscar Bloch. This stimulated me to study the literature on the subject.

A great deal of discussion has been indulged in and a great deal of uncertainty still exists in the minds of surgeons as to who was first to devise this procedure. The consensus of contemporary surgeons seems to favor Mikulicz, since his name is attached to the operation, but a careful study of the literature and correspondence with some leading surgeons in France and elsewhere throw a different light on the question.

Oscar Bloch, on October 20, 1891, read a paper before the Surgical Society of Kopenhagen on "Extra-abdominal Treatment of Intestinal Cancer (with the exception of the rectum)" This lecture appeared in two sections in the Nord Medical Arkiv, 1892, No. 1, og. 8. An abstract of it was also printed in the Zentralblatt f. Chir., 1892, p. 628.

Late in 1892, Reclus published, in collaboration with E. Forgue, in Traité de Therapeutique, two cases of exteriorization of the bowel which he has

Submitted for publication, March 12, 1937.

described. He does not mention Bloch's name. In view of the fact that Bloch's very exhaustive contribution to this subject appeared a year before Reclus' paper, priority for this operation unquestionably should be accorded to Bloch, although in justice to Reclus it must be stated he may have thought of an exteriorization operation without knowing of Bloch's work. This, however, is unlikely because outstanding surgeons such as Reclus usually look up the literature on any procedure they advocate before describing it.

The English accord credit for the exteriorization procedure to one of their own countrymen, E Paul, but Paul published his paper about nine years after the publication of Bloch's lecture; *i.e.,* in the British Medical Journal, February 3, 1900. Paul advised division of the mesocolon, abutment of the proximal and distal loops of the bowel carrying the tumor, with immediate extraperitoneal resection of the tumor mass and the introduction into each end of the bowel of a glass tube to carry off the intestinal contents, without soiling the dressings.

Despite all this, surgeons throughout the world in performing an exteriorization operation refer to it as the "Mikulicz operation." An examination of the facts discloses that Mikulicz published a description of the exteriorization of the bowel in 1902. He also says he had performed this operation since 1898. His operation consists of exteriorizing the bowel, dividing the mesocolon, followed by immediate resection of the tumor. Mikulicz spoke of this procedure in the transactions of the Thirty-second Congress of German Surgeons, in 1902. His procedure is also described by his pupil, W. Anschütz (Beiträge zur Klinik des Dickdarmkrebses. In Mitteilungen aus des Grenzgebieten der Medizin und Chirurgie, 1907. Dritter Supplementband. Gedenkband fur J. Mikulicz). Thus, even though Mikulicz's statement would be found to be correct, *viz.,* that he had performed this operation since 1898, although he reported it in 1902, Bloch would still antedate him by seven years, because Bloch reported his findings to his Surgical Society in 1891.

In 1904, H. Hartman, in Bulletins and Mémoires de la Société Nationale de Chirurgie, Paris, p. 864, published his method of exteriorization, which does not differ from Paul's procedure except in temporary closure of the distal portion of the intestines after resection has been effected.

E. Quénu also exteriorized the bowel but does not claim credit for priority. He attached the leaves of the mesocolon to the parietal peritoneum and resected the involved vascular and lymph supply at the time he removed the tumor. This immediate resection is followed promptly by a partial suturing of the two ends of the intestine for about half their circumference, posteriorly and outside the peritoneum. This technic is described in a thesis by his pupil, Cruet, Paris, 1914, entitled "La meilleure technique operatoire applicable à la method d'exteriorization dans l'extirpation des cancers coliques."

From what has been stated above, one must conclude that credit for the *exteriorization procedure unreservedly belongs to Oscar Bloch and not to Mikulicz.*

I wish to express my appreciation for the cooperation in this study afforded me by Profs. Hartman, Okinczyc, as well as Doctor Leibovici—all of Paris—and for the stimulus of the investigation by Dr. Fred W. Rankin.

MEMOIRS

EDWARD J. KLOPP

1880–1936

Dr. Edward J. Klopp, elected a Fellow of this Association in 1932, died in the Jefferson Hospital on September 19, 1936, after an illness of several

Edward J. Klopp, M.D.

months. The immediate cause of his death was streptococcic endocarditis accompanied by cerebral emboli. This sad and untimely termination of a

life of hard work and brilliant accomplishment was a sad loss to Philadelphia surgery.

Klopp was born in Sheridan, Pa., on June 10, 1880. He was graduated from the Philadelphia College of Pharmacy and Science in 1901 and from the Jefferson Medical College in 1906. He served a two year internship at the Jefferson Hospital and was then made Chief Resident Physician. In 1925, he was given a B.S. degree by the Jefferson Medical College.

He began his surgical career in the service of the late Francis T. Stewart in both the Jefferson and Pennsylvania Hospitals and soon acquired other hospital associations which resulted in a wide and varied surgical experience. In 1928, he was made Associate Professor of Surgery at the Jefferson Medical College, and in 1930, was elected Professor of Surgery. For many years he was Attending Surgeon to the Pennsylvania Hospital, and during his last illness was made Chief of one of the surgical services. At the time of his death he was Attending Surgeon to the Memorial and Delaware County Hospitals and Consultant to the Girard College.

Although not a constant contributor to surgical literature, he wrote a number of brief but valuable papers on intestinal resection, diseases of the breast, on surgery of the thyroid and on blood transfusion. He had performed an unusually large number of colonic and rectal resections for cancer with excellent results. Every surgeon seeing him operate was struck not only with the delicacy and thoroughness of his technic, but with the quiet manner in which he faced and overcame complications and difficulties. He possessed a rare dexterity and gentleness in all his operative work. These qualities were recognized early in his career and resulted in the acquirement of a large surgical practice. In addition to his manual dexterity, Dr. Klopp always displayed a well developed diagnostic knowledge and a sane surgical judgment.

When the United States entered the World War he was made a member of the Medical Advisory Board of Philadelphia. During this period he was doing a large proportion of the surgery at both the Jefferson and Pennsylvania Hospitals.

Although not a brilliant lecturer he was the best kind of teacher. He loved his students and was always kind and helpful to them, and in return, they exhibited for him a respectful appreciation of his sterling qualities.

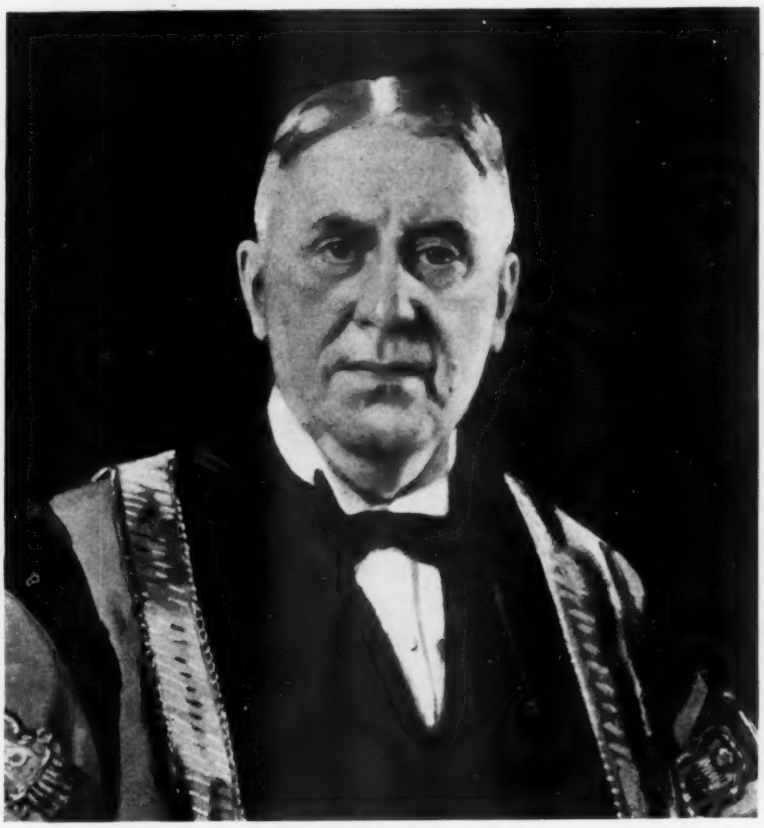
Dr. Klopp was married to Miss Emma Riale, of Johnstown, Pa., in 1911, and she with three daughters and a son survive him.

JOHN H. GIBBON.

LORD MOYNIHAN

1865–1936

BERKELEY GEORGE ANDREW MOYNIHAN was born on the Island of Malta October 2, 1865, and died at his home in Leeds, September 7, 1936. He was the only son of Captain Andrew Moynihan, of Irish stock, who had won the Victoria Cross in the Crimean War at the assault on the Redan. At the



LORD MOYNIHAN, M.D.

time of his son's birth, Captain Moynihan was of the Ninetieth Regiment. Afterwards he was of the Ninth Foot (The King's Regiment), and he served with distinction in the suppression of the Indian Mutiny.

Berkeley Moynihan was educated at the Royal Naval School and received his medical training at the Leeds Medical School and the University of London. He began the clinical part of his studies at the Leeds General Infirmary, in 1886. He took his degree of M.B., B.S., at the University of

London in 1887, with the diplomas of the Royal Colleges. He took the F.R.C.S., in 1890, and in the examination for the degree of Master of Surgery, in 1893, was awarded a gold metal. In 1895, he married Isabella Wellesley Jessop, daughter of T. R. Jessop, F.R.C.S., J.P., of Leeds. To this marriage were born three children, two daughters, and a son.

Leeds for more than 100 years has been one of the leading medical centers of Great Britain. In its great medical school, families have been represented in which the tradition of surgery has been handed from father to son, for example, in the Teale family through three generations, and in the Hey family through two generations. Joseph Priestley (1733–1804), who isolated oxygen, lived and worked at Leeds before coming to America, in 1794.

Moynihan began his professional career at a period when leading surgeons viewed one another as rivals. It is to his everlasting credit that largely as the result of his unceasing efforts they came to consider themselves as fellow workers in a cause. Moynihan stood unfailingly for honest medicine. He fought cults and quackeries, and by his debates in the House of Lords relating to medical legislation he accomplished much to keep English medicine clean.

Moynihan was skilled in many fields of surgery, but particularly in that of abdominal surgery. His work on cancer of the stomach and on ulcer of the stomach and duodenum was outstanding. In 1906, he published his monumental book, Abdominal Operations, which ran through four editions. This book was the most illuminating treatise of its time on abdominal surgery.

Moynihan's association with the Royal College of Surgeons of England was very active. He served on the Council and for six consecutive years he was President of the College. He delivered the Arris and Gale Lectures, 1898–1900; was Hunterian Professor, 1919–1920; Bradshaw Lecturer, in 1920; Hunterian Orator, in 1927. In addition, he was Romanes Lecturer, Oxford, 1932; Walker Lecturer, St. Andrews, 1933, and Linacre Lecturer, Cambridge, 1936. In spite of his engrossing occupations in London, he maintained his home at his beautiful estate in the outskirts of Leeds.

England is stable, and her stability not only is inherent in the character of her people, among whom fanatics are rare, but it is increased by the custom of the English Government of taking into political and social orders the great men of the country in all walks of life. The men thus elevated are given power to use their abilities for the good of society, not by the votes of the uninformed, not by appeal to the emotions of the people, but because of their genuine worth. The superior position conferred is for life, as are appointments to the bench in England and to the Supreme Court in this country. No matter what the background of the man, if he has added greatly by his intelligence to the economic or social welfare of the people, he may be distinguished, and, if one may say so, may become a stockholder in the English hierarchy. He may become in succession, a knight, a baronet, and a baron, as Moynihan so worthily became. As one reviews the life of

Moynihan, one sees manifest in its entire course the qualities in the individual which collectively have made England great and stable.

Lord Moynihan was interested in America. In his many visits to this country, by reason of his scientific presentations in surgery, and at times in the many interesting phases of medicine of the days gone by, he became known and loved by all. He was the supreme speaker in medicine, not only because of his magnetic voice and personality, his polished and beautiful diction, but because of the substance of the ideas he presented. It was not merely knowledge, but knowledge inspired by the wisdom which makes use of knowledge, that made him one of the greatest teachers we have known.

As a member of the House of Lords, Moynihan steadily stressed the necessity of good relationships among all the English speaking peoples, and he pointed out with justifiable pride the fact that between Canada, with its 11,000,000 people, and the United States, with its population of 130,000,000, there are 3,000 miles of frontier, unguarded by forts, without evidence of unrest on either side. The harmony between the two countries has been one of the untold, but nevertheless important, features in international relationships. The feeling behind it is not rooted in a question of trade or material advantage, but is a growing feeling of racial solidarity, which Lord Moynihan recognized and estimated as one which would do much to solidify the English speaking peoples against aggression by war-like nations. Whatever the United States may think about foreign wars, we cannot believe that one which would include aggression against Canada would find the United States unresponsive, nor can we believe that should other English speaking peoples be involved, Canada would be unresponsive to the call of consanguinity.

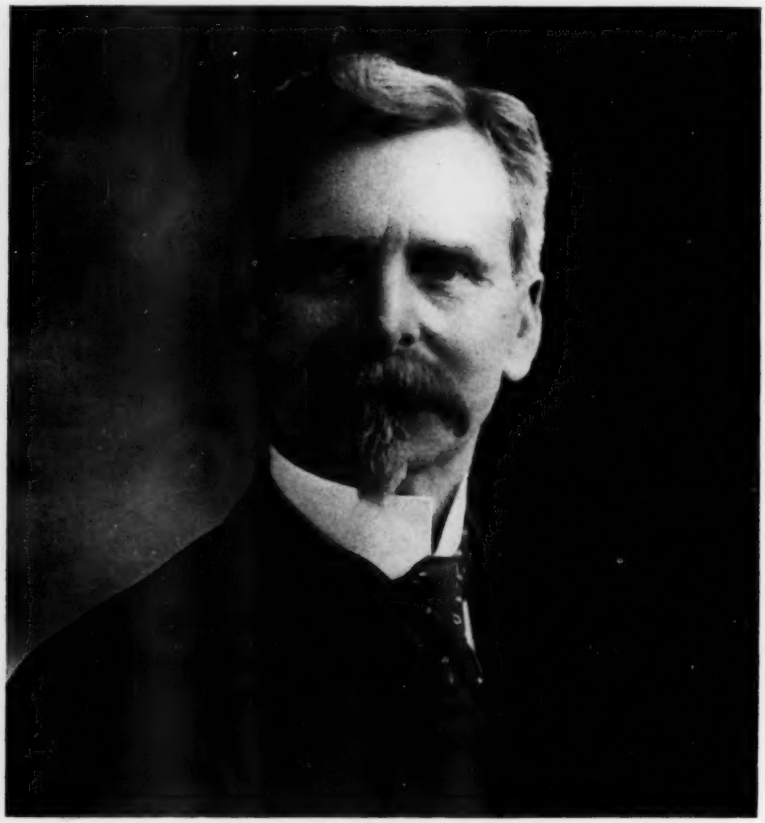
Lord Moynihan, brilliant, versatile, wise and sound, a great surgeon and teacher, will be profoundly missed.

WILLIAM J. MAYO

ISAAC SCOTT STONE

1851–1936

On October 12, 1887, the Southern Surgical and Gynecological Association was founded. Among those who are inscribed as founders is the name of Isaac S. Stone. One by one these distinguished names have disappeared from the list of the Founders and in the last issue of the Transactions only



Isaac Scott Stone, M.D.

the name of Isaac S. Stone remained. On December 22, 1935, he answered the final summons; and his name will appear no more in the list of Fellows and the last of the Founders has gone. He had been a useful, faithful and devoted member of this Association for 48 years.

Doctor Isaac S. Stone was born at Sandy Spring, Md., on March 1, 1851, the son of James H. and Martha A. Scott Stone. Sandy Spring is a small community of cultured families, mostly of the Quaker religious faith, in which denomination Doctor Stone was born and in which he died. His

early youth was spent on a farm on which he labored with marked ability, especially in mechanical lines, until he was 15 years of age. About this time he determined to study medicine and he sought the assistance of his cousin, Dr. D. E. Stone, a prominent physician, who lived near Frederick, Md., with whom he prepared to enter a medical school. Consequently in October, 1870, he matriculated in the medical department of the University of Maryland and following the usual course was graduated in 1872. He was at this time a handsome, affable and courteous young man, just 21 years of age. Having determined to locate in the village of Lincoln, Va., his father is said to have outfitted him with a horse and saddle and but little else. However, he rapidly succeeded in practice and in three years had paid off all his obligations and had married a charming lady of that town. His inclinations were, however, more directed toward gynecology than to general practice and after a few years he went to New York, where he observed the work of Sims, Emmett, Thomas and other pioneers in this specialty and he determined to devote himself to that line of work.

His attainments and his pleasing personality soon began to attract attention and he was appointed a State Medical Examiner of Candidates for Licensure at an early age and was a delegate from the Medical Society of Virginia to the meeting of the Amercian Medical Association, held in New Orleans, in 1885. Two years later, as has been stated, he was one of those who assisted in founding this association, the first annual meeting of which was held in Birmingham, Ala., in December, 1888. At this meeting Doctor Stone was present and read a paper entitled "The Field and Limitation of Laparotomy," in which he enunciated principles of treatment that are universally accepted as correct today. Earlier in this same year, in order to still further perfect himself in gynecology, he left his wife and three small children and went to England to observe the work of Lawson Tait, Mr. Bantock and other great surgeons and he brought back to this country an increased enthusiasm for his work on the diseases of women. He established a hospital in Londen County, Va., but he soon found his location to be unsuited for his specialty and in 1890 he received an appointment to Columbia Hospital for Women in Washington and he moved to that city. Within six months from the time of his arrival in the capital he was elected Clinical Professor of Gynecology in Georgetown University Medical School. He rapidly increased in eminence and in favor and among his many patients was one of the "First Ladies of the Land."

After practising his profession for about 50 years, he resigned his positions in Georgetown University and the Columbia Hospital and was elected Emeritus Professor of Gynecology in the one and Emeritus Surgeon in the other. In 1917, he was elected President of the Southern Surgical Association and served during the ensuing year, presiding at the meeting held in Baltimore, in December, 1918. He was also a member of a number of foreign and local special associations such as The British Gynæcological Society, The Royal Society of Medicine of London, The American Gyneco-

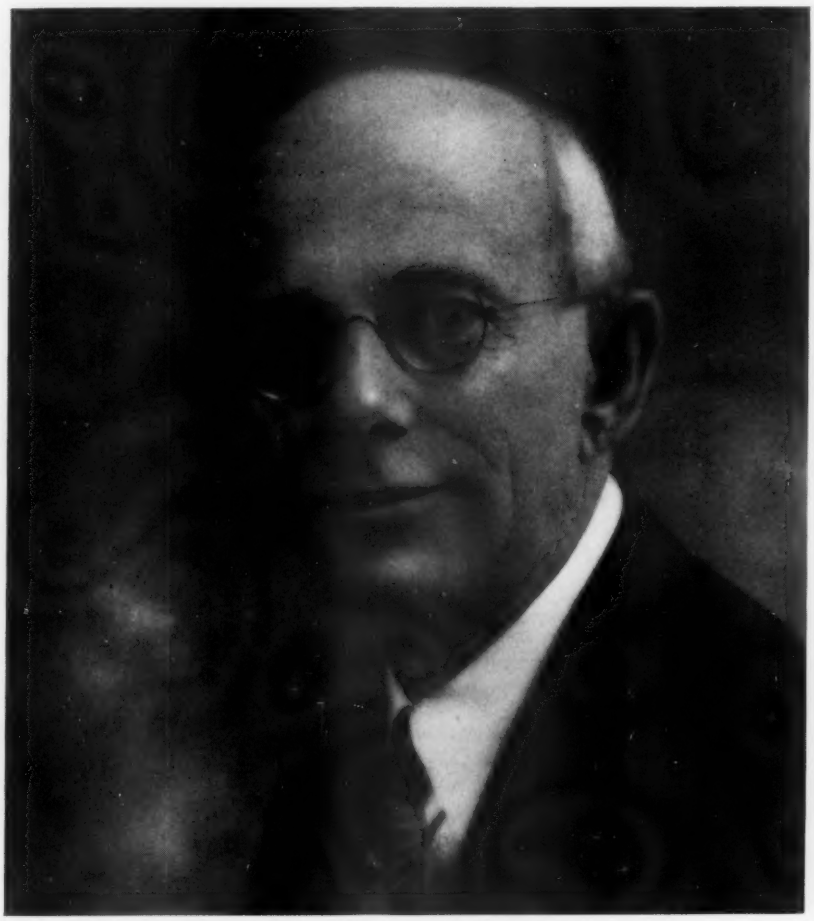
logical Society, and The Washington Surgical Society. He was a faithful attender of the meetings of the Southern Surgical Association and frequently contributed papers and engaged in the discussions of others on such occasions. He was honored by his Alma Mater, the University of Maryland, in 1907, by the bestowal of the honorary degree of Doctor of Science, and, in 1921, Georgetown University conferred on him the degree of Doctor of Laws. Advancing years and increasing infirmities had compelled him to discontinue all professional work for a decade or more before his death, but he was held in high esteem by both his older and younger colleagues; and the writer who had known him since 1871 feels a personal loss in his decease. He was an honest, industrious and worthy man, who had served well in his day and generation—Vale!

RANDOLPH WINSLOW

WILLIAM BURTON THORNING

1872–1937

FEBRUARY 12, 1936, marked the passing of one of our most friendly and beloved surgeons, Dr. William Burton Thorning, who died of coronary occlusion at the age of 63.



WILLIAM BURTON THORNING, M.D.

Doctor Thorning was of sturdy New England stock, being the son of William H. H. and Elizabeth (Knight) Thorning. He was born in Sullivan, N. H., July 2, 1872.

His early education was obtained in the public schools at Keene, N. H., and his medical education at the University of Vermont, from which university he was graduated in 1897.

Following his graduation he was for several years the assistant of the great

surgeon, Dr. Maurice Richardson of Boston, Mass. At the end of this period he left Boston, located and practiced his profession at Winchendon, Mass., where he remained for 11 years doing an active surgical practice. At the end of these years of practice in Massachusetts, he went abroad where he enjoyed postgraduate work in Vienna, London and other clinics in England.

Upon his return to the United States he decided against the rigorous bleak winters of the North and determined to cast his lot with the Southern people, locating at Houston in 1910. He mentioned to me that he rather enjoyed the thought of being in a warmer climate, and among such hospitable people.

It was during his early months in Houston that he visited my operating room and it was from the first he became a friendly and welcome visitor. Our discussions of surgical cases were frequent and profitable.

His warm friendliness and deep interest in the problems of organized medicine soon stamped him as a leader in the ranks of medical workers in Texas.

He was a natural and genial leader and in 1920 was elected Councilor of the Ninth District to later become the Chairman of this body. In this capacity he exerted a fine and tremendous influence, as his medical ideals were of an unusually high order.

In 1916, he and his associates organized the Houston Clinic, which is still carried on by his colleagues.

He was a pleasing and convincing speaker, a writer of ability and captivating style. For many years as Editor-in-Chief of the Medical Records and Annals, he wielded a broad and fine influence in this section of the country.

He was a Charter Member of the Texas Surgical Society, and it was my pleasure to serve with him and Prof. J. E. Thompson as a committee to present those surgeons of Texas who were to compose the Charter Membership. Here the fairness of a fine character and discriminating mind exhibited itself. As a member of this Society he was respected and loved by his Fellows. He was a Fellow of the American Medical Association, a Fellow of the Southern Surgical Association, and a Fellow of the American College of Surgeons. As a member of the State Medical Association of Texas, he was a member of the Committee which rewrote the Constitution and By-Laws in 1924–1925, which Committee produced an instrument said to be one of the most complete of its kind in the country. His interests were not alone confined to medicine but in Civic and State affairs he was very active, always showing a willingness to respond to such calls as were made upon him. He was a thirty-second-degree Mason and a Shriner, being a member of the Arabia Temple Shrine.

Surviving him are his wife, *née* Gertrude M. Goodnow, to whom he was married June 1, 1905, at Keene, N. H., and a son, Dr. Wm. Burton Thorning, Jr., who is now carrying on in the footsteps of his father in the Clinic which his father and his colleagues established so many years ago.

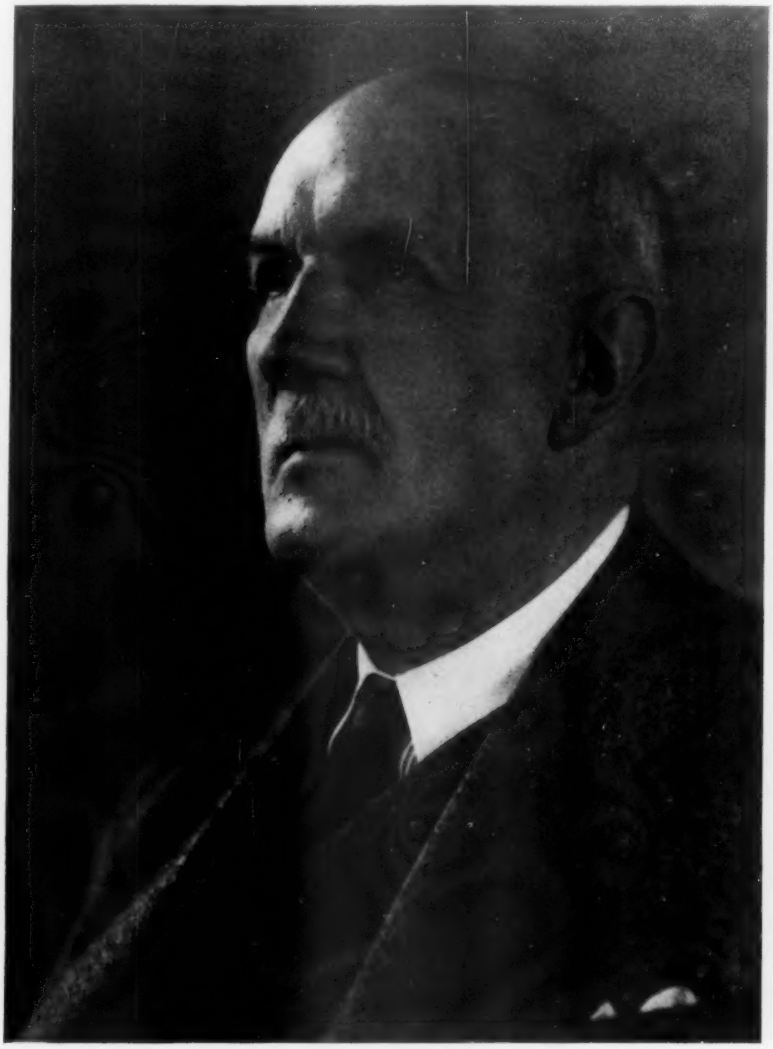
We shall miss the presence of William B. Thorning in the meetings of the Southern Surgical Association and other organizations to which he belonged.

JOHN T. MOORE

JOHN FAIRBAIRN BINNIE

1863–1936

Dr. John Fairbairn Binnie was born in Stirling, Scotland, April 22, 1863, son of Rev. William Binnie, minister of the Reformed Presbyterian



John Fairbairn Binnie, M.D.

Church, who in 1875 went to Aberdeen as Professor of Church History in the Free Church College. Jack Binnie, as they called the son, took his

collegiate degree of A.M. at King's College, Aberdeen, in 1882, and entered the Marischal College of Medicine, being graduated therefrom as M.D. and C.M. in 1886. He had a year's internship in the Royal Infirmary in Glasgow, 1886 and 1887, at a time when William Macewen had a surgical service in the hospital. He later spent some time in Goettingen and Berlin, coming to America in 1889. He entered the practice of surgery in Kansas City, Mo., served for a time as Professor of Surgery in the Kansas State University, and for many years was surgeon to the General Hospital of Kansas City.

Doctor Binnie was elected to fellowship in the American Surgical Association in 1901, and Vice-president in 1907 and 1919. In 1906, he was made a member of the Society of Clinical Surgery and was a member of the Societé Internationale de Chirurgie. In addition to professional societies, Doctor Binnie was a member of the Authors' Club in London, The Kansas City Club and the University Club of Kansas City. Doctor Binnie was one of the founders of the Kansas City Country Club, brought the first golf club to that city, a spoon brassie from Aberdeen. One day when I was in Kansas City, Doctor Binnie took me to the golf course and there showed me a line of ruts across the fairway, explaining that these were made by the wheels of the pioneers going to California, for this was a still recognizable part of the famous Oregon Trail. I could not but take off my hat to the Oregon Trail.

In 1909, at the age of 46, Doctor Binnie married Ellen Mosher.

During the World War, Doctor Binnie organized Base Hospital No. 28 in Kansas City, going with that unit to France, with the rank of major in the Medical Reserve Corps. In 1918, he was promoted to the rank of Lieutenant Colonel, and served as a consultant surgeon to the Third Army Corps. He received a citation for Exceptionally Meritorious and Conspicuous Service at Base Hospital No. 28, France. At this time it was evident to his friends, notably Dr. Harvey Cushing, that Doctor Binnie was suffering from overwork, and they suggested that he be ordered for a rest to Limoges, France, where Base Hospital No. 28 was located, and from there he was ordered home. While waiting for his sailing orders he had a cerebral hemorrhage at Angers, France. He was sent home on a hospital ship and taken to a governmental hospital at Fox Hills until he was well enough to return to Kansas City. In March, 1919, he was able to resume his practice, but in July, 1921, he suffered a second stroke which caused a right hemiplegia.

It was pathetic that one who had lived as much by his pen as by his scalpel, who as a raconteur was a joy to his friends, who was a student of and contributor to medical literature, a skilled operator, should, at the age of 58, be struck down with a cerebral hemorrhage so that thereafter he was unable to read, write or talk, or even move his right hand. Slowly, he recovered sufficiently to walk and to say a few words, but, realizing his condition, he was terribly depressed and discouraged, and when I tried

to assure him that if he would persist in the effort, he could add a worthwhile number of words to his vocabulary, he said very clearly, "What's the use? No hope," and this was, as far as I know, the most that he ever spoke. He was brought to the Letterman Hospital, San Francisco Army Hospital at the Presidio, where he remained from July, 1922, for a year. In 1923, Doctor Binnie had the joy of a visit from Sir William Macewen of Glasgow whom he had admired since his intern days. Shortly thereafter he was sent to the Naval Hospital at San Diego, where he seemed to be comparatively happy, taking an interest in the work of the hospital and enjoying perhaps more than anything else automobile trips about San Diego and vicinity, directing the chauffeur with his hand. For four years he lived in the city of San Diego, until his death, November 28, 1936.

Doctor Binnie was much beloved by a large circle of friends and had the respect and affection of his fellows in the American Surgical Association. For a number of years he went to Rochester, Minn., at Christmas time, and put on wig and false beard to act as Santa Claus for the children of Dr. William J. Mayo.

I last saw Doctor Binnie in May, 1936, at his home in San Diego. Although he was suffering severely, he had himself lifted into a wheel chair and brought out from his bedroom into the living room where we had a little visit, "reminiscing" about old days, and in spite of his pain and his limited vocabulary, he could not resist the temptation to make a gesticulatory joke at my expense.

The California State Medical Association at its meeting in San Diego in 1929 held a special meeting to honor Doctor Binnie, who was present and who was deeply touched by the attention. Dr. William J. Mayo presided and gave an address wherein he called attention to the fact that in Binnie's "Operative Surgery" the commoner operations are described briefly, but if one seeks the detail of some unusual or difficult operation, he is very apt to find it in "Binnie." Doctor Binnie contributed many articles to professional journals of muscles, tendons and bursae, and in 1905 put out his own Manual of Operative Surgery, a small pocket-sized edition in which his sense of humor cropped out every now and then; *e.g.,* in the preface he referred the reader for references to the literature of operative surgery to the index catalog of the Surgeon General's Office. The book has gone through many editions; the final (8th) edition was a great octavo volume of 1300 pages. In all these editions upwards of 50,000 copies were printed. I understand from Mrs. Binnie that there is a movement on foot to produce another revised edition, bringing it up to date. It was a close rival and worthy successor of Jacobson, which in its day was by far the best Operative Surgery in the English language.

On August 4, 1915, Doctor Binnie gave a lecture before the California Academy of Medicine in San Francisco, his subject being, "The Rôle of the Sympathetic in Symptoms of Abdominal Disease," a very early and telling paper in the discussion of the surgery of the sympathetic system,

which has become so prominent in recent medical practice and literature.

In 1917, Doctor Binnie served as editor of a Treatise on Regional Surgery, 3 volumes, Blakiston, in which he personally contributed much in the field of operative surgery; he also wrote the chapters on Congenital Defects, Hernia, and Diseases of the Abdominal Wall.

In 1909, Doctor Binnie suggested and worked for a diagnostic department at Research Hospital, Kansas City; some 15 years afterwards these suggestions bore fruit, and such an institution was founded and gotten under way, and is now flourishing. The Diagnostic Department at Research Hospital was opened formally with a ceremony, the Department being made possible through a gift of $75,000 by William Volker.

Doctor Binnie is buried in Fort Rosecrans National Cemetery, San Diego, Calif.

EMMET RIXFORD.

EDITORIAL ADDRESS

Original typed manuscripts and illustrations submitted to this Journal should be forwarded prepaid, at the author's risk, to the Chairman of the Editorial Board of the ANNALS OF SURGERY

Walter Estell Lee, M.D

1833 Pine Street, Philadelphia, Pa.

Contributions in a foreign language when accepted will be translated and published in English.

Exchanges and Books for Review should be sent to James T. Pilcher, M.D., Managing Editor, 121 Gates Avenue, Brooklyn, N. Y.

Subscriptions, advertising and all business communications should be addressed

ANNALS OF SURGERY

227 South Sixth Street, Philadelphia, Pa.